8/3/05 10/725,277

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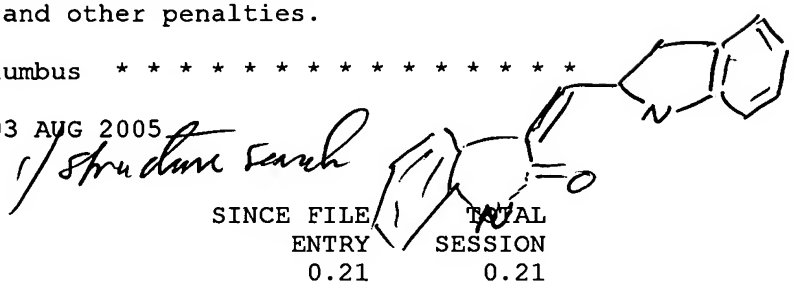
FILE 'HOME' ENTERED AT 14:20:28 ON 03 AUG 2005



1/structure search

=> fil reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 14:20:37 ON 03 AUG 2005
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 2 AUG 2005 HIGHEST RN 857941-82-3
DICTIONARY FILE UPDATES: 2 AUG 2005 HIGHEST RN 857941-82-3

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

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**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,   *
* effective March 20, 2005.  A new display format, IDERL, is now    *
* available and contains the CA role and document type information. *
*                                                                    *
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Structure search iteration limits have been increased. See HELP SLIMITS for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

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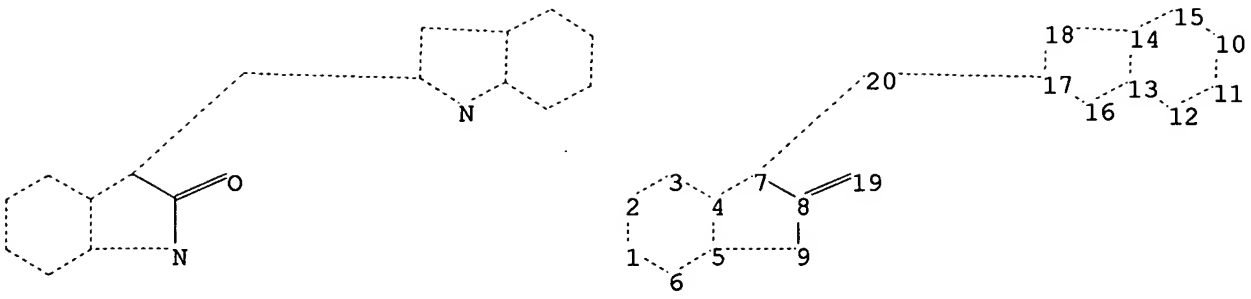
Uploading C:\Program Files\Stnexp\Queries\10725277\10725277f.str



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19 20
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18
chain bonds :
7-20 8-19 17-20
ring bonds :
1-2 1-6 2-3 3-4 4-5 4-7 5-6 5-9 7-8 8-9 10-11 10-15 11-12 12-13 13-14
13-16 14-15 14-18 16-17 17-18
exact/norm bonds :
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Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:CLASS
20:CLASS

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=> d
L1 HAS NO ANSWERS
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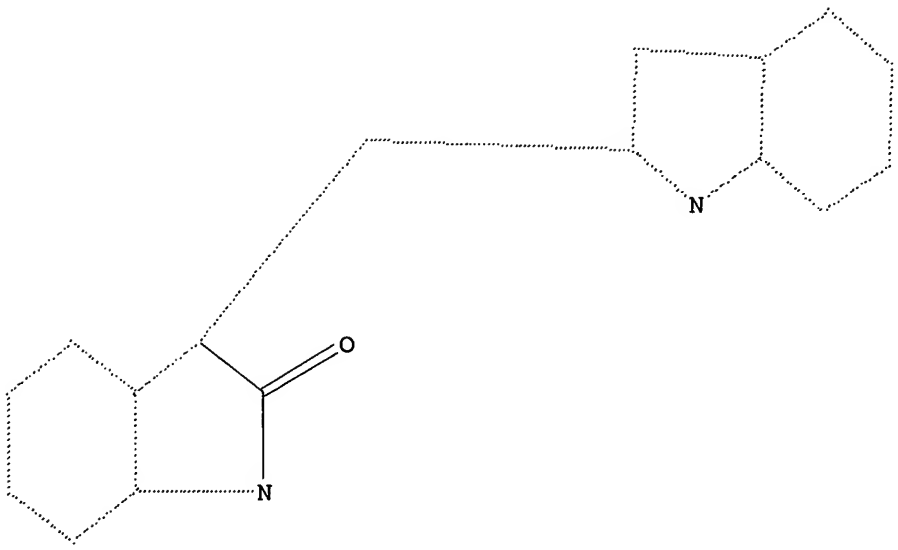

Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SCREEN SEARCH COMPLETED -    224 TO ITERATE

100.0% PROCESSED      224 ITERATIONS                          17 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:         3583 TO     5377
PROJECTED ANSWERS:              93 TO      587

L2           17 SEA SSS SAM L1

=> s L1 full
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100.0% PROCESSED     4296 ITERATIONS                         322 ANSWERS
SEARCH TIME: 00.00.01

L3           322 SEA SSS FUL L1

=> fil caplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                               161.76     161.97

FILE 'CAPLUS' ENTERED AT 14:21:42 ON 03 AUG 2005
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FILE COVERS 1907 - 3 Aug 2005 VOL 143 ISS 6
FILE LAST UPDATED: 2 Aug 2005 (20050802/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s L3
L4 35 L3

=> d ibib abs hitstr

L4 ANSWER 1 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:614538 CAPLUS
TITLE: Real time electronic cell sensing systems and applications for cell-based assays
INVENTOR(S): Xu, Xiao; Abassi, Yama; Wang, Xiaobo; Gan, Jiangbo
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 66 pp., Cont.-in-part of U.S. Ser. No. 705,447.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005153425	A1	20050714	US 2004-987732	20041112
WO 2004010102	A2	20040129	WO 2003-US22537	20030718
WO 2004010102	A3	20040722		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004152067	A1	20040805	US 2003-705615	20031110
US 2005112544	A1	20050526	US 2003-705447	20031110

PRIORITY APPLN. INFO.:

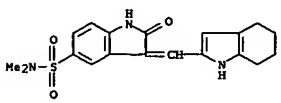
US 2002-435400P	P	20021220
US 2003-469572P	P	20030509
WO 2003-US22537	A	20030718
US 2003-705447	A2	20031110
US 2003-705615	A2	20031110
US 2003-519567P	P	20031112
US 2004-542927P	P	20040209
US 2004-548713P	P	20040227
US 2002-397749P	P	20020720
WO 2003-US22557	A	20030718

AB The present invention includes devices, systems, and methods for assaying cells using cell-substrate impedance monitoring. In one aspect, the invention provides cell-substrate impedance monitoring devices that comprise electrode arrays on a nonconducting substrate, in which each of the arrays has an approx. uniform electrode resistance across the entire array. In another aspect, the invention provides cell-substrate monitoring systems comprising one or more cell-substrate monitoring devices comprising multiple wells each having an electrode array, an impedance analyzer, a device station that connects arrays of individual wells to the impedance analyzer, and software for controlling the device station and impedance analyzer. In another aspect, the invention provides cellular assays that use impedance monitoring to detect changes in cell behavior or state. In some preferred aspects, the assays are designed to investigate the affects of compds. on cells, such as cytotoxicity assays. In other preferred aspects, the assays are designed to investigate the compds. that effect IgE-mediated responses of cells to antigens.

IT 330161-87-0, SU6656
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(electronic cell sensing systems and applications for cell-based assays)

L4 ANSWER 1 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

RN 330161-87-0 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N,N-dimethyl-2-oxo-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



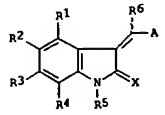
=> d ibib abs hitstr 2-35

L4 ANSWER 2 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:567120 CAPLUS
DOCUMENT NUMBER: 143:97259
TITLE: Preparation of indolinone derivatives as agents to prevent, treat and/or ameliorate multiple sclerosis.
INVENTOR(S): Bouerat, Laetitia Maud Elysa; Fensholdt, Jaf; Nielsen, Simon Feldbaek; Liang, Xifu; Havez, Sophie Elisabeth; Andersson, Ellen Christina; Jensen, Lene; Hansen, Jens Rainer
PATENT ASSIGNEE(S): Leo Pharma A/S, Den.
SOURCE: PCT Int. Appl., 198 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005058309	A1	20050630	WO 2004-DK875	20041216

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-529630P P 20031216
GI



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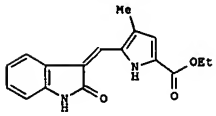
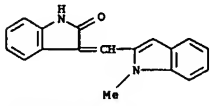


II

AB Title compds. I [R1-4 = H, halo, trihalomethyl, etc.; R5 = H, OH, alkyl, etc.; R6 = H, alkyl, cycloalkyl, etc.; A = Ph, mono/bicyclic heteroaryl,

L4 ANSWER 2 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
etc.; X = O, S] are prepd. For instance, II is prepd. from 5-formyl-4-methyl-1H-pyrrole-2-carboxylic acid Et ester and 1,3-dihydroindol-2-one (EtOH, piperidine) in 99% yield. In an assay of exptl.-induced autoimmune encephalomyelitis (EAE) compds. of the invention, in particular, 3-(3,5-dimethyl-1H-pyrrol-2-ylmethylene)-1,3-dihydroindol-2-one (no exptl.), is shown to significantly inhibit EAE compared to dexamethasone; both compds. are known KDR kinase inhibitors. I are useful for the prevention, treatment or amelioration of multiple sclerosis, or to delay the onset of or reduce the relapse rate in multiple sclerosis.
IT 856436-18-5P, 3-(1-Methyl-1H-indol-2-ylmethylene)-1,3-dihydroindol-2-one
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of indolinone derivs. as agents to inhibit exptl.-induced autoimmune encephalomyelitis)
RN 856436-18-5 CAPLUS
CN INDEX NAME NOT YET ASSIGNED



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:516338 CAPLUS
DOCUMENT NUMBER: 143:55640
TITLE: Identifying, selecting and/or characterizing compounds which modulate the activity of an Src family kinase
INVENTOR(S): Obermeier, Axel; Bieger, Boris
PATENT ASSIGNEE(S): Sirenade Pharmaceuticals AG, Germany
SOURCE: Eur. Pat. Appl., 114 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1541694	A1	20050615	EP 2003-28713	20031212

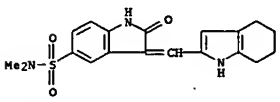
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

WO 2005059168	A1	20050630	WO 2004-EP53321	20041207

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2003-28713 A 20031212
AB The invention relates to a method of identifying, selecting and/or characterizing a compound which modulates the activity of at least one Src family kinase. The method comprises (a) cultivating a cell or cell line containing at least one nucleic acid coding for a Src family kinase or a mutated Src family kinase under suitable conditions, (b) expressing the nucleic acid(s) in the cell(s), (c) contacting the cell(s) of step (b) with at least one test compds., and (d) determining whether the phenotype of the
cell(s) of step (c) is changed as compared with the phenotype of the cell(s) of step (b). Preferably, the invention employs at least one Src family kinase mutation which leads to a hyperactive form of a Src family kinase and, moreover, exhibits a mutation which allows determination of the specificity and binding mode of a test compds ("double mutant type"). Thus, in human Src kinase, a critical lysine-298 in the ATP-binding consensus
site of the tyrosine kinase domain is mutated to alanine, thereby abolishing ATP binding, and allowing use as a control for compound-mode-of-action. Threonine-341 in the ATP binding site may be mutated to glutamine, and tyrosine-530 is mutated to phenylalanine, resulting in a hyperactive form of Src. Displaying the most dramatic phenotypic response, cell lines expressing Src-Y530F seem ideally suited to establish a method enabling a highly parallel and quant. readout of the readily observable phenotype changes and their suppression by potential Src inhibitory test compds. For reasons of classification of novel inhibitors according to their mode of action and specificity, the SRC-TQ/YF and SRC-KA expressing cell lines may be employed. Suppression of biol. responses by the chemical compds. PP1-Chr, SU6656, PP2, geldanamycin, 17-AAG, and radicicol provide proof-of-principle. The invention further relates to compds. identified by said method,

L4 ANSWER 3 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
pharmaceutical compns. and the use of those compds. and pharmaceutical compns. in the treatment of diseases, which are at least in part caused by a Src family kinase.
IT 330161-87-0, SU6656
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(identifying, selecting and/or characterizing compds. which modulate the activity of an Src family kinase)
RN 330161-87-0 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N,N-dimethyl-2-oxo-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:451524 CAPLUS
DOCUMENT NUMBER: 142:478368
TITLE: Real time electronic cell sensing systems and applications for cell-based assays
INVENTOR(S): Xu, Xiao; Abbassi, Yama; Wang, Xiaobo; Gan, Jiangbo
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 161 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005047482	A2	20050526	WO 2004-US37696	20041112
WO 2005047482	A3	20050707		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

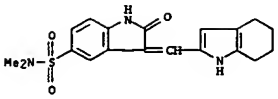
PRIORITY APPLN. INFO.: US 2003-519567P P 20031112
US 2004-542927P P 20040209
US 2004-548713P P 20040227

AB The present invention includes devices, systems, and methods for assaying cells using cell-substrate impedance monitoring. In one aspect, the invention provides cell-substrate impedance monitoring devices that comprise electrode arrays on a nonconducting substrate, in which each of the arrays has an approx. uniform electrode resistance across the entire array. In another aspect, the invention provides cell-substrate monitoring systems comprising one or more cell-substrate monitoring devices comprising multiple wells each having an electrode array, an impedance analyzer, a device station that connects arrays of individual wells to the impedance analyzer, and software for controlling the device station and impedance analyzer. In another aspect, the invention provides cellular assays that use impedance monitoring to detect changes in cell behavior or state.

IT 330161-87-0, SU6656
RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(target src; real time electronic cell sensing systems and applications for cell-based assays)

RN 330161-87-0 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N,N-dimethyl-2-oxo-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)

L4 ANSWER 4 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



L4 ANSWER 5 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN

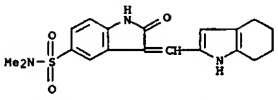
ACCESSION NUMBER: 2005:423985 CAPLUS
DOCUMENT NUMBER: 143:5153
TITLE: The membrane cytoskeletal crosslinker ezrin is required for metastasis of breast carcinoma cells
AUTHOR(S): Elliott, Bruce E.; Meens, Jalna A.; SenGupta, Sandip K.; Louvard, Daniel; Arpin, Monique
CORPORATE SOURCE: Division of Cancer Biology and Genetics, Cancer Research Institute, Queen's University, Kingston, ON, Can.
SOURCE: Breast Cancer Research (2005), 7(3), R365-R373
CODEN: BRCRFS; ISSN: 1465-542X
URL: http://breast-cancer-research.com/content/pdf/bcr1006.pdf
PUBLISHER: BioMed Central Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Introduction: The membrane cytoskeletal crosslinker ezrin participates in several functions including cell adhesion, motility and cell survival, and there is increasing evidence that it regulates tumor progression. However, the role played by ezrin in breast cancer metastasis has not been clearly delineated. Methods: We examined the role of ezrin in metastasis using a highly metastatic murine mammary carcinoma cell line, namely AC2M2. Stable cell clones that overexpress wild-type ezrin or a dominant-neg. amino-terminal domain of ezrin were selected. They were then tested for cell motility and invasion in vitro, and metastasis in a mouse in vivo tumor transplantation model. Results: Parental AC2M2 cells and cells overexpressing wild-type ezrin were transplanted into the mammary fat pad of syngeneic recipient mice; these animals subsequently developed lung metastases. In contrast, expression of the dominant-neg. amino-terminal ezrin domain markedly inhibited lung metastasis. Consistent with this effect, we observed that the expression of amino-terminal ezrin caused strong membrane localization of cadherin, with increased cell-cell contact and a decrease in cell motility and invasion, whereas cells expressing wild-type ezrin exhibited strong cytoplasmic expression of cadherins and pseudopodia extensions. In addition, inhibitors of phosphatidylinositol 3-kinase and c-Src significantly blocked cell motility and invasion of AC2M2 cells expressing wild-type ezrin. We further found that overexpression of amino-terminal ezrin reduced levels of Akt pS473 and cytoskeletal-associated c-Src pY418 in AC2M2 cells, which contrasts with the high levels of phosphorylation of these proteins in cells expressing wild-type ezrin. Phosphorylated Erk1/2 was also reduced in amino-terminal ezrin expressing cells, although a mitogen-activated protein kinase kinase (MEK) inhibitor had no detectable effect on cell motility or invasion in this system. Conclusion: Our findings indicate that ezrin is required for breast cancer metastasis, and that c-Src and phosphatidylinositol 3-kinase/Akt are effectors of ezrin in the cell motility and invasion stages of the metastatic process. Together, these results suggest that blocking ezrin function may represent a novel and effective strategy for preventing breast cancer metastasis.

IT 330161-87-0, SU6656
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(c-Src was required for ezrin-mediated cell motility and invasion of metastatic murine breast carcinoma AC2M2 cell line evident by attenuation of cell motility by c-Src inhibitor SU6656)

RN 330161-87-0 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N,N-dimethyl-2-oxo-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)

L4 ANSWER 5 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:416371 CAPLUS
DOCUMENT NUMBER: 143:1108
TITLE: Inhibition of neuronal apoptosis by the cyclin-dependent kinase inhibitor GW8510: Identification of 3' substituted indolones as a scaffold for the development of neuroprotective drugs
AUTHOR(S): Johnson, Kyle; Liu, Li; Majdzadeh, Nazanin; Chavez, Cindy; Chin, Paul C.; Morrison, Brad; Wang, Lulu; Park, Jane; Chugh, Priti; Chen, Hsin-Mei; D'Mello, Santosh R.
CORPORATE SOURCE: Department of Molecular and Cell Biology, University of Texas at Dallas, Richardson, TX, USA
SOURCE: Journal of Neurochemistry (2005), 93(3), 538-548
CODEN: JONRA9; ISSN: 0022-3042
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

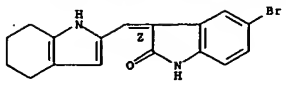
AB Increasing evidence suggests that neuronal apoptosis is triggered by the inappropriate activation of cyclin-dependent kinases leading to an abortive re-entry of neurons into the cell cycle. Pharmacol. inhibitors of cell-cycle progression may therefore have value in the treatment of neurodegenerative diseases in humans. GW8510 is a 3' substituted indolone that was developed recently as an inhibitor of cyclin-dependent kinase 2 (CDK2). We found that GW8510 inhibits the death of cerebellar granule neurons caused by switching them from high potassium (HK) medium to low potassium (LK) medium. Although GW8510 inhibits CDK2 and other CDKs when tested in in vitro biochem. assays, when used on cultured neurons it only inhibits CDK5, a cytoplasmic CDK that is not associated with cell-cycle progression. Treatment of cultured HEK293T cells with GW8510 does not inhibit cell-cycle progression, consistent with its inability to inhibit mitotic CDKs in intact cells. Neuroprotection by GW8510 is independent of Akt and MEK-ERK signaling. Furthermore, GW8510 does not block the LK-induced activation of Gsk3β and, while inhibiting c-jun phosphorylation, does not inhibit the increase in c-jun expression observed in apoptotic neurons. We also examined the effectiveness of other 3' substituted indolone compds. to protect against neuronal apoptosis. We found that like GW8510, the VEGF Receptor 2 Kinase Inhibitors [3-(1H-pyrrol-2-ylmethylene)-1,3-dihydroindol-2-one], (Z)-3-2,4-Dimethyl-3-(ethoxycarbonyl)pyrrol-5-ylmethylidenylindol-2-one and [(Z)-5-Bromo-3-(4,5,6,7-tetrahydro-1H-indol-2-ylmethylene)-1,3-dihydroindol-2-one], the Src family kinase inhibitor SU6656 and a com. available inactive structural analog of an RNA-dependent protein kinase inhibitor 5-Chloro-3-(3,5-dichloro-4-hydroxybenzylidene)-1,3-dihydro-indol-2-one, are all neuroprotective when tested on LK-treated neurons. Along with our recent identification of the c-Raf inhibitor GW5074 (also a 3' substituted indolone) as a neuroprotective compound, our findings identify the 3' substituted indolone as a core structure for the designing of neuroprotective drugs that may be used to treat neurodegenerative diseases in humans.

IT **288144-20-7 330161-87-0**, SU6656
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(action of CDKs inhibitor GW8510 and other 3' substituted indolone compds. in protection protect against neuronal apoptosis)

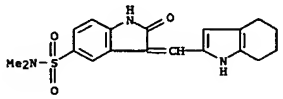
RN 288144-20-7 CAPLUS
CN 2H-Indol-2-one, 5-bromo-1,3-dihydro-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

L4 ANSWER 6 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 330161-87-0 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N,N-dimethyl-2-oxo-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN

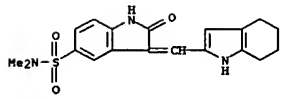
ACCESSION NUMBER: 2005:311513 CAPLUS
DOCUMENT NUMBER: 142:476084
TITLE: Src family kinase inhibitors block amphiregulin-mediated autocrine ErbB signaling in normal human keratinocytes
AUTHOR(S): Kansra, Sanjay; Stoll, Stefan W.; Johnson, Jessica L.; Elder, James T.
CORPORATE SOURCE: Department of Dermatology, University of Michigan Medical Center, Ann Arbor, MI, USA
SOURCE: Molecular Pharmacology (2005), 67(4), 1145-1157
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB C-Src potentiates proliferation, survival, and invasiveness in response to epidermal growth factor (EGF) in human mammary carcinoma cells. Tyrosine (Tyr) 845 of ErbB1 is phosphorylated by Src and has been implicated in control of malignant behavior. Although several lines of evidence also suggest important interactions of ErbB and Src family kinase signaling in normal epithelial cells, little is known about the mechanism of this interaction. Studying normal human keratinocytes (NHKs), here we demonstrate strong expression of the Src family kinases Src, Yes, and Fyn; Src family kinase-dependent stimulation of Tyr 845 by EGF; and potent inhibition of NHK proliferation and migration by two Src family kinase inhibitors PP1 and PD173952. EGF-stimulated extracellular signal-regulated kinase (ERK) phosphorylation occurred at much lower concns. of EGF than required to phosphorylate Tyr 845. Moreover, the effect of Src family kinase inhibitors on EGF-stimulated ERK phosphorylation was transient, prompting a search for other targets of Src family kinase action. By ELISA anal., we found that three different Src family kinase inhibitors [6-(2,6-dichlorophenyl)-8-methyl-2-(4-morpholin-4-ylphenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one (PD173952), 4-amino-5-(4-methylphenyl)-7-(t-butyl)pyrazolo[3,4-D]pyrimidine (PP1), and 2-oxo-3-(4,5,6,7-tetrahydro-1H-indol-2-ylmethylene)-2,3-dihydro-1H-indole-5-sulfonic acid dimethylamide (SU6656)] markedly inhibited elaboration of soluble amphiregulin by NHKs. The ErbB inhibitor PD158780 and the mitogen-activated protein kinase kinase inhibitor U0126 also markedly inhibited NHK proliferation, migration, and amphiregulin production Together, these observations demonstrate that one or more Src family kinases act upstream as well as downstream of ErbB1 to promote amphiregulin-dependent autocrine stimulation of NHKs and suggest that autocrine NHK proliferation is more dependent upon ERK activation than upon Tyr 845 phosphorylation.

IT **330161-87-0**, SU6656
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Src family kinase inhibitors block amphiregulin-mediated autocrine ErbB signaling in normal human keratinocytes)

RN 330161-87-0 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N,N-dimethyl-2-oxo-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)

L4 ANSWER 7 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

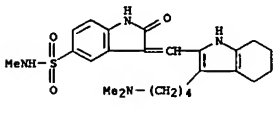
L4 ANSWER 8 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:265986 CAPLUS
DOCUMENT NUMBER: 142:475250
TITLE: QSAR studies of amino propyl tetrahydro indole based indolin-2-ones as potent inhibitor of Src tyrosine kinase
AUTHOR(S): Kumar, B. Ashok; Ramasree, D.; Parthasarathy, T.; Uma, V.
CORPORATE SOURCE: Computational Chemistry Lab, Department of Chemistry, Nizam College, Osmania University, Hyderabad, 500 001, India
SOURCE: Journal of Teaching and Research in Chemistry (2004), 11(2), 20-24
CODEN: JTRCEN; ISSN: 0971-6408
PUBLISHER: Dr. R. C. Samanta Roy Institute of Science & Technology
DOCUMENT TYPE: Journal
LANGUAGE: English

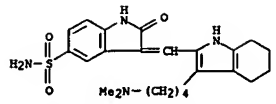
AB A series of substituted 3-[3-(aminopropyl)-4,5,6,7-tetrahydro-1-H-indole-2-ylmethylene]-1, 3-dihydro-2-ones as potent inhibitors of the non-receptor tyrosine kinase Src was quant. analyzed in terms of physicochem. parameters by regression anal. The predictive potential of the model was discussed on the basis of lipophilicity parameter, QlogP and the steric parameter, MR as the descriptor variable. Sulfone moiety was found to be essential for potency towards Src inhibition.

IT 852159-05-8 852159-06-9 852159-07-0
852159-08-1 852159-09-2 852159-10-5
852159-11-6 852159-12-7 852159-13-8
852159-14-9 852159-15-0 852159-16-1
852159-17-2 852159-18-3
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(QSAR based on lipophilicity parameter, QlogP, steric parameter and MR showed that amino Pr tertahydro indole based indolinone derivative sulfone
moiety to be essential for potency towards Src inhibition)

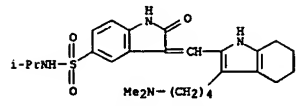
RN 852159-05-8 CAPLUS
CN 1H-Indole-5-sulfonamide, 3-[[3-[4-(dimethylamino)butyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylene]-2,3-dihydro-N-methyl-2-oxo- (9CI) (CA INDEX NAME)



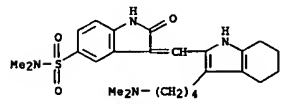
RN 852159-06-9 CAPLUS
CN 1H-Indole-5-sulfonamide, 3-[[3-[4-(dimethylamino)butyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylene]-2,3-dihydro-2-oxo- (9CI) (CA INDEX NAME)



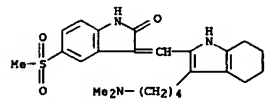
RN 852159-07-0 CAPLUS
CN 1H-Indole-5-sulfonamide, 3-[[3-[4-(dimethylamino)butyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylene]-2,3-dihydro-N-(1-methylethyl)-2-oxo- (9CI) (CA INDEX NAME)



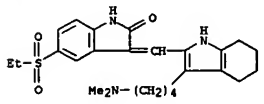
RN 852159-08-1 CAPLUS
CN 1H-Indole-5-sulfonamide, 3-[[3-[4-(dimethylamino)butyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylene]-2,3-dihydro-N,N-dimethyl-2-oxo- (9CI) (CA INDEX NAME)



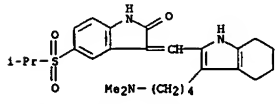
RN 852159-09-2 CAPLUS
CN 2H-Indol-2-one, 3-[[3-[4-(dimethylamino)butyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylene]-1,3-dihydro-5-(methylsulfonyl)- (9CI) (CA INDEX NAME)



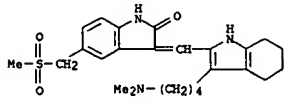
RN 852159-10-5 CAPLUS
CN 2H-Indol-2-one, 3-[[3-[4-(dimethylamino)butyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylene]-5-(ethylsulfonyl)-1,3-dihydro- (9CI) (CA INDEX NAME)



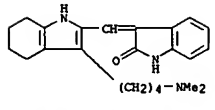
RN 852159-11-6 CAPLUS
CN 2H-Indol-2-one, 3-[[3-[4-(dimethylamino)butyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylene]-1,3-dihydro-5-[(1-methylethyl)sulfonyl]- (9CI) (CA INDEX NAME)



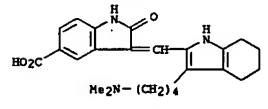
RN 852159-12-7 CAPLUS
CN 2H-Indol-2-one, 3-[[3-[4-(dimethylamino)butyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylene]-1,3-dihydro-5-[(methylsulfonyl)methyl]- (9CI) (CA INDEX NAME)



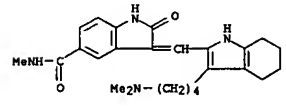
RN 852159-13-8 CAPLUS
CN 2H-Indol-2-one, 3-[[3-[4-(dimethylamino)butyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)



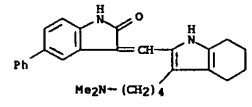
RN 852159-14-9 CAPLUS
CN 1H-Indole-5-carboxylic acid, 3-[[3-[4-(dimethylamino)butyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylene]-2,3-dihydro-2-oxo- (9CI) (CA INDEX NAME)



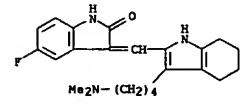
RN 852159-15-0 CAPLUS
CN 1H-Indole-5-carboxamide, 3-[[3-[4-(dimethylamino)butyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylene]-2,3-dihydro-N-methyl-2-oxo- (9CI) (CA INDEX NAME)



RN 852159-16-1 CAPLUS
CN 2H-Indol-2-one, 3-[[3-[4-(dimethylamino)butyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylene]-1,3-dihydro-5-phenyl- (9CI) (CA INDEX NAME)

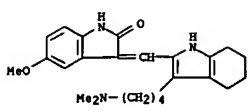


RN 852159-17-2 CAPLUS
CN 2H-Indol-2-one, 3-[[3-[4-(dimethylamino)butyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylene]-5-fluoro-1,3-dihydro- (9CI) (CA INDEX NAME)



RN 852159-18-3 CAPLUS
CN 2H-Indol-2-one, 3-[[3-[4-(dimethylamino)butyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylene]-1,3-dihydro-5-methoxy- (9CI) (CA INDEX NAME)

L4 ANSWER 8 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:66903 CAPLUS
DOCUMENT NUMBER: 142:148787
TITLE: Methods for treating diseases and disorders related to unregulated angiogenesis and/or vasculogenesis
INVENTOR(S): Tang, Peng Cho; Sun, Li; Shawver, Laura Kay; Hirth, Klaus Peter; Fong, Annie
PATENT ASSIGNEE(S): Sugen, Inc., USA
SOURCE: U.S., 40 pp., Cont.-in-part of U.S. 6,147,106.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6846839	B1	20050125	US 1999-333703	19990616
US 5880141	A	19990309	US 1995-485323	19950607
CN 1155838	A	19970730	CN 1996-190616	19960605
US 5792783	A	19980811	US 1996-655223	19960605
US 5883116	A	19990316	US 1996-655224	19960605
US 5883113	A	19990316	US 1996-659191	19960605
US 5886020	A	19990323	US 1996-655226	19960605
EP 934931	A2	19990811	EP 1999-103667	19960605
EP 934931	A3	19991020		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
JP 2000026412	A2	20000125	JP 1999-159567	19960605
US 6147106	A	20001114	US 1997-915366	19970820
EP 1247803	A2	20021009	EP 2002-77564	19970820
EP 1247803	A3	20021016		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 2002022626	A1	20020221	US 2000-617529	20000713
US 2003108946	A1	20030612	US 2002-76621	20020219
US 2004067531	A1	20040408	US 2003-458730	20030611

PRIORITY APPLN. INFO.:

US 1995-485323	A2	19950607
US 1996-655223	A2	19960605
US 1996-655224	A2	19960605
US 1996-655226	A2	19960605
US 1996-655255	B2	19960605
US 1996-659191	A2	19960605
US 1996-702232	B2	19960823
US 1997-915366	A2	19970820
EP 1996-918093	A3	19960605
JP 1997-501363	A3	19960605
US 1996-31585P	P	19961205
US 1996-31586P	P	19961205
US 1996-31588P	P	19961205
US 1996-32546P	P	19961205
US 1996-32547P	P	19961205
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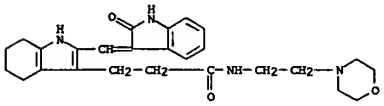
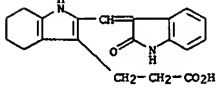
US 1997-46843P	P	19970505
EP 1997-939480	A3	19970820
US 1998-129256	B1	19980804

L4 ANSWER 9 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
US 2000-617529 B1 20000713
OTHER SOURCE(S): MARPAT 142:148787
AB The present invention relates to methods for treating diseases and disorders related to unregulated angiogenesis and/or vasculogenesis. More specifically, this invention relates to methods for treating diseases and disorders, such as rheumatoid arthritis, endometriosis, ocular neovascularization, solid tumor growth and metastases, and excessive scarring during wound healing, with indolinone compds. The indolinones inhibit growth factor-stimulated cell proliferation.
IT **245036-28-6P 245036-29-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(methods for treating diseases and disorders related to unregulated angiogenesis and/or vasculogenesis using indolinones that inhibit growth factor-stimulated cell proliferation)
RN 245036-28-6 CAPLUS
CN 1H-Indole-3-propanamide, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4,5,6,7-tetrahydro-N-[2-(4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 245036-29-7 CAPLUS
CN 1H-Indole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 231 THERE ARE 231 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:2190 CAPLUS
DOCUMENT NUMBER: 142:93676
TITLE: A preparation of sulfonamide substituted indolinones, useful as inhibitors of DNA dependent protein kinase (DNA-PK)
INVENTOR(S): Howlett, Anthony R.; Rice, Audie; Moshinsky, Deborah; Hammarsten, Ola
PATENT ASSIGNEE(S): Sugen, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 46 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004266843	A1	20041230	US 2004-793943	20040308

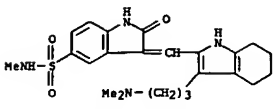
PRIORITY APPLN. INFO.:

US 2003-452549P	P	20030307

OTHER SOURCE(S): MARPAT 142:93676
GI

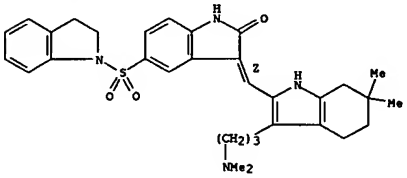
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to a preparation of sulfonamide substituted indolinones of formula I [wherein: R1 and R2 are independently selected from H, (un)substituted Ph, thiazolyl, or alkyl, etc.; R3, R4, and R5 are independently selected from H or alkyl], useful as inhibitors of DNA dependent protein kinase (DNA-PK). The invention relates to the field of radiosensitizing agents which are capable of enhancing radiotherapy by inhibiting DNA-PK (DNA-protein kinase). For instance, sulfonamide substituted indolinone II was prepared via condensation of pyrrole derivative III and indole derivative IV. The prepared indolinone derivative V was found to inhibit DNA-PK (IC50 = 1.6 μM).
IT **666235-61-6P 775321-71-6P 775321-76-1P**
775321-87-4P 775321-88-5P 775321-89-6P
775321-90-9P 775322-02-6P 775322-03-7P
775322-04-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of sulfonamide substituted indolinones useful as inhibitors of DNA dependent protein kinase (DNA-PK))
RN 666235-61-6 CAPLUS
CN 1H-Indole-5-sulfonamide, 3-[[3-[3-(dimethylamino)propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylene]-2,3-dihydro-N-methyl-2-oxo- (9CI) (CA INDEX NAME)



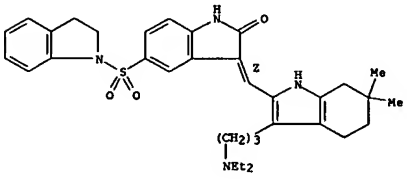
RN 775321-71-6 CAPLUS
CN 1H-Indole, 1-[[(3Z)-3-[[3-[3-(dimethylamino)propyl]-4,5,6,7-tetrahydro-6,6-dimethyl-1H-indol-2-yl]methylene]-2,3-dihydro-2-oxo-1H-indol-5-yl]sulfonyl]-2,3-dihydro- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



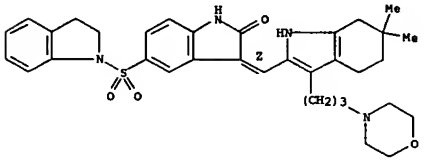
RN 775321-76-1 CAPLUS
CN 1H-Indole, 1-[[(3Z)-3-[[3-[3-(diethylamino)propyl]-4,5,6,7-tetrahydro-6,6-dimethyl-1H-indol-2-yl]methylene]-2,3-dihydro-2-oxo-1H-indol-5-yl]sulfonyl]-2,3-dihydro- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



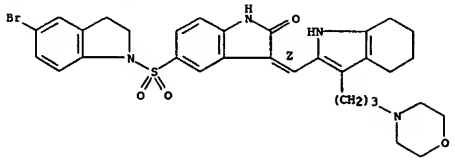
RN 775321-87-4 CAPLUS
CN 1H-Indole, 1-[[(3Z)-2,3-dihydro-2-oxo-3-[[4,5,6,7-tetrahydro-3-[3-(1-pyrrolidinyl)propyl]-1H-indol-2-yl]methylene]-1H-indol-5-yl]sulfonyl]-2,3-dihydro- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



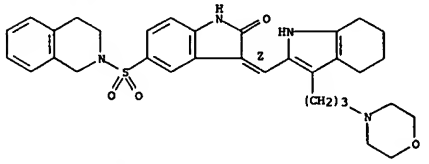
RN 775322-02-6 CAPLUS
CN 1H-Indole, 5-bromo-1-[[(3Z)-2,3-dihydro-2-oxo-3-[[4,5,6,7-tetrahydro-3-[3-(4-morpholinyl)propyl]-1H-indol-2-yl]methylene]-1H-indol-5-yl]sulfonyl]-2,3-dihydro- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



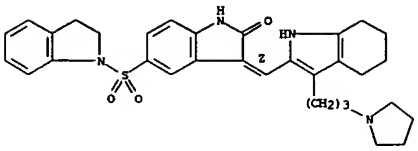
RN 775322-03-7 CAPLUS
CN Isoquinoline, 2-[[(3Z)-2,3-dihydro-2-oxo-3-[[4,5,6,7-tetrahydro-3-[3-(4-morpholinyl)propyl]-1H-indol-2-yl]methylene]-1H-indol-5-yl]sulfonyl]-1,2,3,4-tetrahydro- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



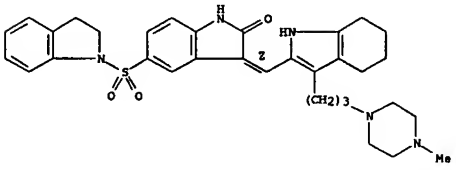
RN 775322-04-8 CAPLUS
CN Quinoline, 1-[[(3Z)-2,3-dihydro-2-oxo-3-[[4,5,6,7-tetrahydro-3-[3-(4-morpholinyl)propyl]-1H-indol-2-yl]methylene]-1H-indol-5-yl]sulfonyl]-1,2,3,4-tetrahydro- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



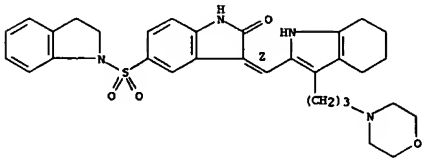
RN 775321-88-5 CAPLUS
CN 1H-Indole, 1-[[(3Z)-2,3-dihydro-2-oxo-3-[[4,5,6,7-tetrahydro-3-[3-(4-methyl-1-piperazinyl)propyl]-1H-indol-2-yl]methylene]-1H-indol-5-yl]sulfonyl]-2,3-dihydro- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



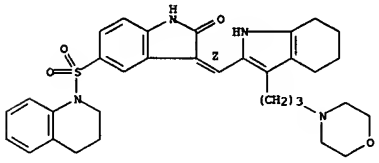
RN 775321-89-6 CAPLUS
CN 1H-Indole, 1-[[(3Z)-2,3-dihydro-2-oxo-3-[[4,5,6,7-tetrahydro-3-[3-(4-morpholinyl)propyl]-1H-indol-2-yl]methylene]-1H-indol-5-yl]sulfonyl]-2,3-dihydro- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 775321-90-9 CAPLUS
CN 1H-Indole, 1-[[(3Z)-2,3-dihydro-2-oxo-3-[[4,5,6,7-tetrahydro-6,6-dimethyl-3-[3-(4-morpholinyl)propyl]-1H-indol-2-yl]methylene]-1H-indol-5-yl]sulfonyl]-2,3-dihydro- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

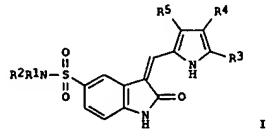


L4 ANSWER 11 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN

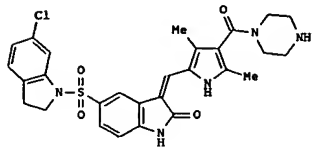
ACCESSION NUMBER: 2004:857170 CAPLUS
DOCUMENT NUMBER: 141:350032
TITLE: Preparation of 5-sulfonamido-substituted indolinone compounds as protein kinase inhibitors
INVENTOR(S): Tang, Peng Cho; Liang, Congxin; Miller, Todd; Lipson, Kenneth E.
PATENT ASSIGNEE(S): Sugen Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 58 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004204407	A1	20041014	US 2004-793952		20040308
PRIORITY APPLN. INFO.:			US 2003-452552P	P	20030307

OTHER SOURCE(S): MARPAT 141:350032
GI



I



II

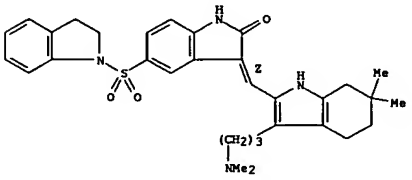
AB The title compds. [I; R1 and R2 combine to form (un)substituted optionally fused heterocyclic ring; R3-R5 = H, alkyl, hydroxyalkyl, etc.; or R3 and R4 may combine to form a cyclic 6-membered alicyclic ring which may be substituted with one or more lower alkyl] that modulate the activity of protein kinases ("PKs") and are therefore useful in treating disorders related to abnormal PK activity (no biol. data), were prepared General method of synthesis of the compds. I by condensation of oxindoles and aldehydes (preparation of intermediates is given) is described. Eighty-two compds. I (e.g., II) were prepared Pharmaceutical compns. comprising the compds. I, methods of treating diseases utilizing pharmaceutical compns. comprising these compds. and methods of preparing them are also disclosed.

L4 ANSWER 11 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

IT 775321-71-6P 775321-76-1P 775321-87-4P
775321-88-5P 775321-89-6P 775321-90-9P
775322-02-6P 775322-03-7P 775322-04-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 5-sulfonamido-substituted indolinone compds. as protein kinase inhibitors)

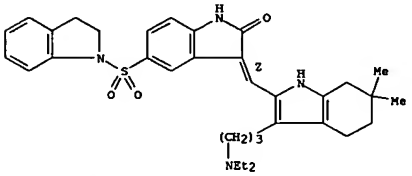
RN 775321-71-6 CAPLUS
CN 1H-Indole, 1-[[(3Z)-3-[[3-[3-(dimethylamino)propyl]-4,5,6,7-tetrahydro-6,6-dimethyl-1H-indol-2-yl]methylene]-2,3-dihydro-2-oxo-1H-indol-5-yl]sulfonyl]-2,3-dihydro- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 775321-76-1 CAPLUS
CN 1H-Indole, 1-[[(3Z)-3-[[3-[3-(diethylamino)propyl]-4,5,6,7-tetrahydro-6,6-dimethyl-1H-indol-2-yl]methylene]-2,3-dihydro-2-oxo-1H-indol-5-yl]sulfonyl]-2,3-dihydro- (9CI) (CA INDEX NAME)

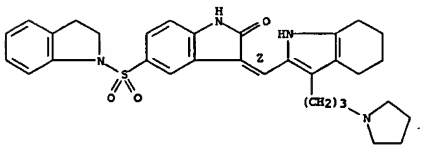
Double bond geometry as shown.



RN 775321-87-4 CAPLUS
CN 1H-Indole, 1-[[(3Z)-2,3-dihydro-2-oxo-3-[[4,5,6,7-tetrahydro-3-[3-(1-pyrrolidinyl)propyl]-1H-indol-2-yl]methylene]-1H-indol-5-yl]sulfonyl]-2,3-dihydro- (9CI) (CA INDEX NAME)

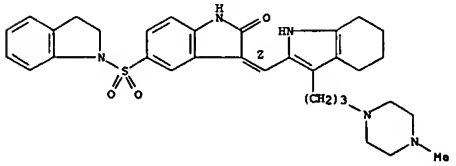
Double bond geometry as shown.

L4 ANSWER 11 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



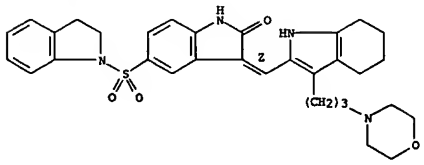
RN 775321-88-5 CAPLUS
CN 1H-Indole, 1-[[(3Z)-2,3-dihydro-2-oxo-3-[[4,5,6,7-tetrahydro-3-[3-(4-methyl-1-piperazinyl)propyl]-1H-indol-2-yl]methylene]-1H-indol-5-yl]sulfonyl]-2,3-dihydro- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 775321-89-6 CAPLUS
CN 1H-Indole, 1-[[(3Z)-2,3-dihydro-2-oxo-3-[[4,5,6,7-tetrahydro-3-[3-(4-morpholinyl)propyl]-1H-indol-2-yl]methylene]-1H-indol-5-yl]sulfonyl]-2,3-dihydro- (9CI) (CA INDEX NAME)

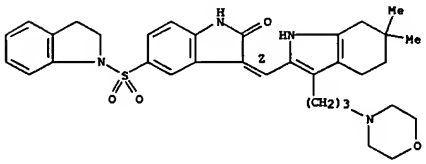
Double bond geometry as shown.



RN 775321-90-9 CAPLUS
CN 1H-Indole, 1-[[(3Z)-2,3-dihydro-2-oxo-3-[[4,5,6,7-tetrahydro-6,6-dimethyl-3-[3-(4-morpholinyl)propyl]-1H-indol-2-yl]methylene]-1H-indol-5-yl]sulfonyl]-2,3-dihydro- (9CI) (CA INDEX NAME)

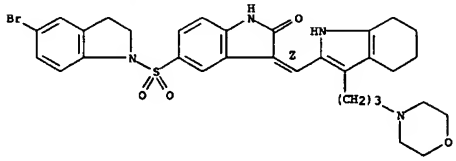
Double bond geometry as shown.

L4 ANSWER 11 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



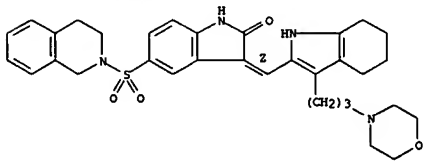
RN 775322-02-6 CAPLUS
CN 1H-Indole, 5-bromo-1-[[(3Z)-2,3-dihydro-2-oxo-3-[[4,5,6,7-tetrahydro-3-[3-(4-morpholinyl)propyl]-1H-indol-2-yl]methylene]-1H-indol-5-yl]sulfonyl]-2,3-dihydro- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 775322-03-7 CAPLUS
CN Isoquinoline, 2-[[(3Z)-2,3-dihydro-2-oxo-3-[[4,5,6,7-tetrahydro-3-[3-(4-morpholinyl)propyl]-1H-indol-2-yl]methylene]-1H-indol-5-yl]sulfonyl]-1,2,3,4-tetrahydro- (9CI) (CA INDEX NAME)

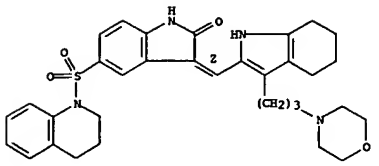
Double bond geometry as shown.



RN 775322-04-8 CAPLUS
CN Quinoline, 1-[[(3Z)-2,3-dihydro-2-oxo-3-[[4,5,6,7-tetrahydro-3-[3-(4-morpholinyl)propyl]-1H-indol-2-yl]methylene]-1H-indol-5-yl]sulfonyl]-1,2,3,4-tetrahydro- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

L4 ANSWER 11 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



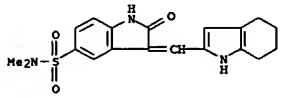
L4 ANSWER 12 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:419904 CAPLUS
DOCUMENT NUMBER: 142:70669
TITLE: Characterization of a Conserved Structural Determinant Controlling Protein Kinase Sensitivity to Selective Inhibitors
AUTHOR(S): Blencke, Stephanie; Zech, Birgit; Engkvist, Ola; Greff, Zoltan; Orfi, Laszlo; Horvath, Zoltan; Keri, Gyoergy; Ullrich, Axel; Daub, Henrik
CORPORATE SOURCE: Axxima Pharmaceuticals AG, Munchen, 81377, Germany
SOURCE: Chemistry & Biology (2004), 11(5), 691-701
CODEN: CBOLE2; ISSN: 1074-5521
PUBLISHER: Cell Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Some protein kinases are known to acquire resistance to selective small mol. inhibitors upon mutation of a conserved threonine at the ATP binding site to a larger residue. Here, we performed a comprehensive mutational anal. of this structural element and determined the cellular sensitivities of several disease-relevant tyrosine kinases against various inhibitors. Mutant kinases possessing a larger side chain at the critical site showed resistance to most compds. tested, such as ZD1839, PP1, AG1296, STI571, and a pyrido[2,3-d]pyrimidine inhibitor. In contrast, indolinones affected both wild-type and mutant kinases with similar potencies. Resistant mutants were established for pharmacol. anal. of βPDGF receptor-mediated signaling and allowed the generation of a drug-inducible system of cellular Src kinase activity. Our data establish a conserved structural determinant of protein kinase sensitivity relevant for both signal transduction research and drug development.

IT 330161-87-0, SU6656
RL: BSU (Biological study, unclassified); BIOL (Biological study) (characterization of a conserved structural determinant controlling protein kinase inhibitor sensitivity)

RN 330161-87-0 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N,N-dimethyl-2-oxo-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN

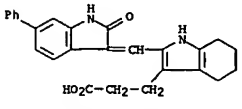
ACCESSION NUMBER: 2004:182368 CAPLUS
DOCUMENT NUMBER: 140:229401
TITLE: Three hybrid assay system for isolating ligand-binding polypeptides and for isolating small mol. ligands
INVENTOR(S): Come, Jon H.; Becker, Frank; Kley, Nikolai A.; Reichel, Christoph
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 238 pp., Cont.-in-part of U.S. Ser. No. 91,177.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004043388	A1	20040304	US 2002-234985		20020903
US 2003165873	A1	20030904	US 2002-91177		20020304
US 2004266854	A1	20041230	US 2004-820453		20040407
PRIORITY APPLN. INFO.:			US 2001-272932P	P	20010302
			US 2001-278233P	P	20010323
			US 2001-329437P	P	20011015
			US 2002-91177	A2	20020304
			US 2001-336962P	P	20011203
			WO 2002-US6677	A2	20020304
			US 2002-234985	A2	20020903
			WO 2002-US33052	A2	20021015
			US 2003-460921P	P	20030407
			US 2003-531872P	P	20031223

AB The invention provides compns. and methods for isolating ligand-binding polypeptides for a user-specified ligand, and for isolating small mol. ligands for a user-specified target polypeptide using an improved class of hybrid ligand compds. Preparation of compds., e.g a methotrexate moiety linked by a polyethylene gycol moiety to dexamethasone, is described.

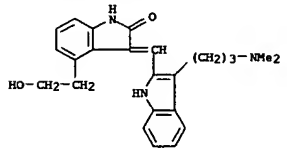
IT 245036-16-2D, conjugates 258830-51-2D, conjugates
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(three hybrid assay system for isolating ligand-binding polypeptides and for isolating small mol. ligands)

RN 245036-16-2 CAPLUS
CN 1H-Indole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-6-phenyl-3H-indol-3-ylidene)methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)



RN 258830-51-2 CAPLUS
CN 2H-Indol-2-one, 3-[[3-[3-(dimethylamino)propyl]-1H-indol-2-yl]methylene]-1,3-dihydro-4-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)

L4 ANSWER 13 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

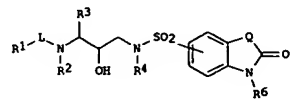


L4 ANSWER 14 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:162694 CAPLUS
DOCUMENT NUMBER: 140:210820
TITLE: Broad spectrum substituted oxindole sulfonamide HIV protease inhibitors
INVENTOR(S): Tahri, Abdellah; Wigerinck, Piet Tom Bert Paul
PATENT ASSIGNEE(S): Tibotec Pharmaceuticals Ltd., Ire.
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004016619	A1	20040226	WO 2003-EP50379	20030814
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2493940	AA	20040226	CA 2003-2493940	20030814
BR 2003005771	A	20041005	BR 2003-5771	20030814
EP 1546153	A1	20050629	EP 2003-787818	20030814
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRIORITY APPLN. INFO.:			EP 2002-78384	A 20020814
			WO 2003-EP50379	W 20030814
OTHER SOURCE(S):	MARPAT 140:210820			

GI



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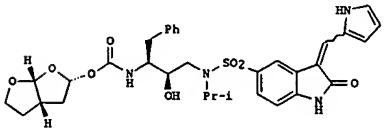
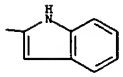


II

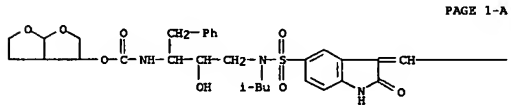
L4 ANSWER 14 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

PAGE 1-B

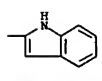


RN 664344-28-9 CAPLUS
CN Carbamic acid, [3-[[[2,3-dihydro-3-(1H-indol-2-ylmethylene)-2-oxo-1H-indol-5-yl]sulfonyl](2-methylpropyl)amino]-2-hydroxy-1-(phenylmethyl)propyl]-, hexahydrofuro[2,3-b]furan-3-yl ester (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

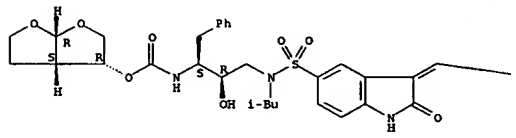
AB The present invention concerns the compds. having the formula (I) N-oxides, salts, stereoisomeric forms, racemic mixts., prodrugs, esters, and metabolites thereof [wherein R1, R8 = H, C1-6 alkyl, C2-6 alkenyl, C3-7 cycloalkyl, aryl, Het1, Het1-C1-6 alkyl, etc.; or R1 = (un)substituted H2N-CH2CH; t is 0, 1 or 2; R2 = H, C1-6 alkyl; L = CO, O-CO, NR8CO, O-C1-6 alkanediyl-CO, NR8-C1-6alkanediyl-CO, SO2, O-SO2, NR8-SO2; R3 = (un)substituted C1-6 alkyl, aryl, C3-7 cycloalkyl, C3-7 cycloalkyl-C1-4 alkyl, aryl-C1-4alkyl; R4 = H, C1-4 alkyl-O-CO, carboxyl, CONH2, mono- or di(C1-4alkyl)carbamoyl, C3-7 cycloalkyl, C2-6 alkenyl, C2-6 alkynyl; R6 = H, (un)substituted C1-6 alkyl; Het1 is a 5 to 10 ring membered mono- or bicyclic heterocycle containing ≥1 heteroatoms selected from N, O, and S]. It further relates to their use as broad spectrum HIV protease inhibitors, pharmaceutical compns., and a method for treating or combating infection or disease associated with multi-drug resistant retrovirus infection in a mammal. It also may concern combinations thereof with another anti-retroviral agent, and to their use in assays as reference compds. or as reagents. These compds. I exhibited potent anti-HIV activity against a wild type laboratory HIV strain (HIV-1 strain L-AI), e.g. sec50 of 8.5 for the compound (II), and also were effective in inhibiting a broad range of mutant strains which show various degrees of phenotypic cross-resistance to the currently com. available drugs such as for instance saquinavir, ritonavir, nelfinavir, indinavir and amprenavir.

IT 664344-08-5 664344-28-9
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(substituted oxindolesulfonamide derivs. for use as broad spectrum HIV protease inhibitors)

RN 664344-08-5 CAPLUS
CN Carbamic acid, [(1S,2R)-3-[[[2,3-dihydro-3-(1H-indol-2-ylmethylene)-2-oxo-1H-indol-5-yl]sulfonyl](2-methylpropyl)amino]-2-hydroxy-1-(phenylmethyl)propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (9CI) (CA INDEX NAME)

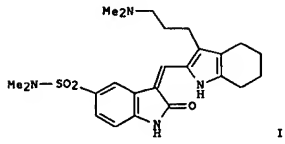
Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A



L4 ANSWER 15 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:981475 CAPLUS
DOCUMENT NUMBER: 140:217468
TITLE: Design and synthesis of aminopropyl tetrahydroindole-based indolin-2-ones as selective and potent inhibitors of Src and Yes tyrosine kinase
AUTHOR(S): Guan, Huiping; Laird, A. Douglas; Blake, Robert A.; Tang, Cho; Liang, Chris
CORPORATE SOURCE: Department of Chemistry, SUGEN, Inc., South San Francisco, CA, 94080, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(1), 187-190
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

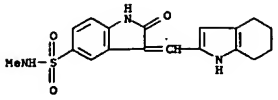


I

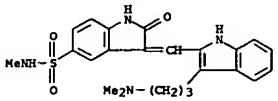
AB A novel series of substituted 3-[3-(aminopropyl)-4,5,6,7-tetrahydro-1H-indol-2-ylmethylene]-1,3-dihydro-indole-2-ones, e.g., I, was discovered as potent inhibitors of the non-receptor tyrosine kinase Src and Yes. A structure-activity relationship was developed in order to optimize their potency and selectivity. Syntheses of these compds. are also described herein.

IT 203991-89-3P 258830-49-8P 258830-99-8P
666235-61-6P 666235-62-7P 666235-63-8P
666235-64-9P 666235-65-0P 666235-66-1P
666235-67-2P 666235-68-3P 666235-69-4P
666235-70-7P 666235-71-8P 666235-72-9P
666235-73-0P 666235-74-1P 666235-75-2P
666235-76-3P 666235-78-5P 666235-79-6P
666235-80-9P 666235-81-0P 666235-82-1P
666235-83-2P 666235-84-3P 666235-85-4P
666235-86-5P 666235-87-6P 666235-88-7P
666235-89-8P 666235-90-1P 666235-91-2P
666235-92-3P 666235-93-4P 666235-94-5P
666235-95-6P 666235-96-7P 666235-97-8P
666235-98-9P 666235-99-0P 666236-00-6P
666236-01-7P 666236-02-8P 666236-03-9P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation, Src and Yes tyrosine kinase inhibitory activity, and structure-activity relationship of aminopropyl tetrahydroindole-based indolinones)

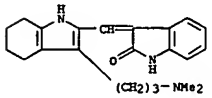
RN 203991-89-3 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N-methyl-2-oxo-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



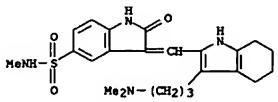
RN 258830-49-8 CAPLUS
CN 1H-Indole-5-sulfonamide, 3-[[3-[3-(dimethylamino)propyl]-1H-indol-2-yl]methylene]-2,3-dihydro-N-methyl-2-oxo- (9CI) (CA INDEX NAME)



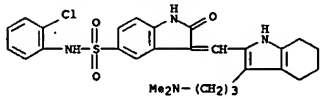
RN 258830-99-8 CAPLUS
CN 2H-Indol-2-one, 3-[[3-[3-(dimethylamino)propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)



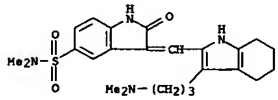
RN 666235-61-6 CAPLUS
CN 1H-Indole-5-sulfonamide, 3-[[3-[3-(dimethylamino)propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylene]-2,3-dihydro-N-methyl-2-oxo- (9CI) (CA INDEX NAME)



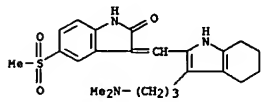
RN 666235-62-7 CAPLUS
CN 1H-Indole-5-sulfonamide, 3-[[3-[3-(dimethylamino)propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylene]-2,3-dihydro-2-oxo- (9CI) (CA INDEX NAME)



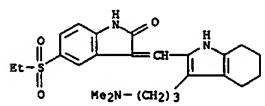
RN 666235-67-2 CAPLUS
CN 1H-Indole-5-sulfonamide, 3-[[3-[3-(dimethylamino)propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylene]-2,3-dihydro-N,N-dimethyl-2-oxo- (9CI) (CA INDEX NAME)



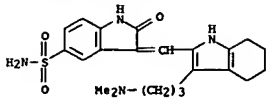
RN 666235-68-3 CAPLUS
CN 2H-Indol-2-one, 3-[[3-[3-(dimethylamino)propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylene]-1,3-dihydro-5-(methylsulfonyl)- (9CI) (CA INDEX NAME)



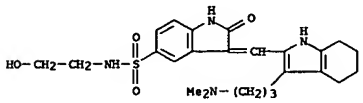
RN 666235-69-4 CAPLUS
CN 2H-Indol-2-one, 3-[[3-[3-(dimethylamino)propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylene]-5-(ethylsulfonyl)-1,3-dihydro- (9CI) (CA INDEX NAME)



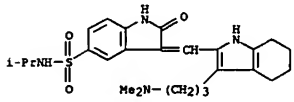
RN 666235-70-7 CAPLUS
CN 2H-Indol-2-one, 3-[[3-[3-(dimethylamino)propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylene]-1,3-dihydro-5-[(1-methylethyl)sulfonyl]- (9CI) (CA INDEX NAME)



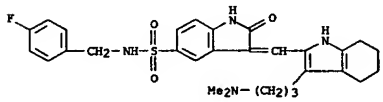
RN 666235-63-8 CAPLUS
CN 1H-Indole-5-sulfonamide, 3-[[3-[3-(dimethylamino)propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylene]-2,3-dihydro-N-(2-hydroxyethyl)-2-oxo- (9CI) (CA INDEX NAME)



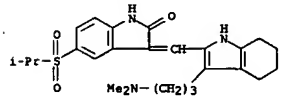
RN 666235-64-9 CAPLUS
CN 1H-Indole-5-sulfonamide, 3-[[3-[3-(dimethylamino)propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylene]-2,3-dihydro-N-(1-methylethyl)-2-oxo- (9CI) (CA INDEX NAME)



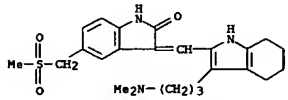
RN 666235-65-0 CAPLUS
CN 1H-Indole-5-sulfonamide, 3-[[3-[3-(dimethylamino)propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylene]-N-[(4-fluorophenyl)methyl]-2,3-dihydro-2-oxo- (9CI) (CA INDEX NAME)



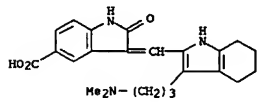
RN 666235-66-1 CAPLUS
CN 1H-Indole-5-sulfonamide, N-(2-chlorophenyl)-3-[[3-[3-(dimethylamino)propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylene]-2,3-dihydro-2-oxo- (9CI) (CA INDEX NAME)



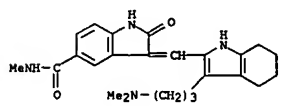
RN 666235-71-8 CAPLUS
CN 2H-Indol-2-one, 3-[[3-[3-(dimethylamino)propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylene]-1,3-dihydro-5-[(methylsulfonyl)methyl]- (9CI) (CA INDEX NAME)



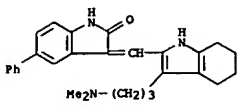
RN 666235-72-9 CAPLUS
CN 1H-Indole-5-carboxylic acid, 3-[[3-[3-(dimethylamino)propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylene]-2,3-dihydro-2-oxo- (9CI) (CA INDEX NAME)



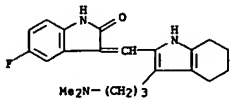
RN 666235-73-0 CAPLUS
CN 1H-Indole-5-carboxamide, 3-[[3-[3-(dimethylamino)propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylene]-2,3-dihydro-N-methyl-2-oxo- (9CI) (CA INDEX NAME)



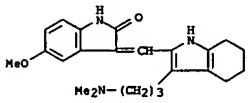
RN 666235-74-1 CAPLUS
CN 2H-Indol-2-one, 3-[[3-[3-(dimethylamino)propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylene]-1,3-dihydro-5-phenyl- (9CI) (CA INDEX NAME)



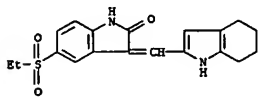
RN 666235-75-2 CAPLUS
CN 2H-Indol-2-one, 3-[[3-[3-(dimethylamino)propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylene]-5-fluoro-1,3-dihydro- (9CI) (CA INDEX NAME)



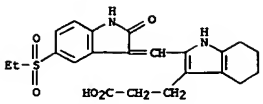
RN 666235-76-3 CAPLUS
CN 2H-Indol-2-one, 3-[[3-[3-(dimethylamino)propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylene]-1,3-dihydro-5-methoxy- (9CI) (CA INDEX NAME)



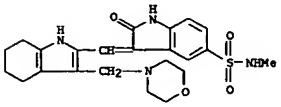
RN 666235-78-5 CAPLUS
CN 2H-Indol-2-one, 5-(ethylsulfonyl)-1,3-dihydro-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



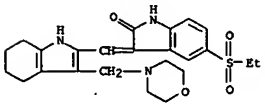
RN 666235-79-6 CAPLUS
CN 1H-Indole-3-propanoic acid, 2-[[5-(ethylsulfonyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)



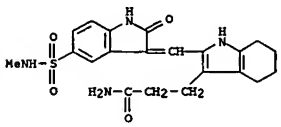
RN 666235-80-9 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N-methyl-2-oxo-3-[[4,5,6,7-tetrahydro-3-(4-morpholinylmethyl)-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)



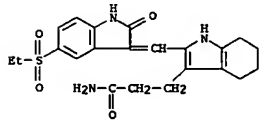
RN 666235-81-0 CAPLUS
CN 2H-Indol-2-one, 5-(ethylsulfonyl)-1,3-dihydro-3-[[4,5,6,7-tetrahydro-3-(4-morpholinylmethyl)-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)



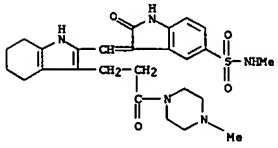
RN 666235-82-1 CAPLUS
CN 1H-Indole-3-propanamide, 2-[[1,2-dihydro-5-[(methylamino)sulfonyl]-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)



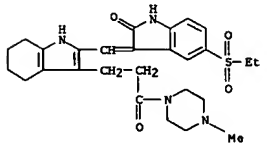
RN 666235-83-2 CAPLUS
CN 1H-Indole-3-propanamide, 2-[[5-(ethylsulfonyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)



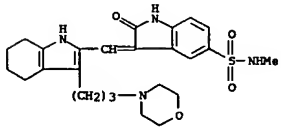
RN 666235-84-3 CAPLUS
CN Piperazine, 1-[3-[2-[[1,2-dihydro-5-[(methylamino)sulfonyl]-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro-1H-indol-3-yl]-1-oxopropyl]-4-methyl- (9CI) (CA INDEX NAME)



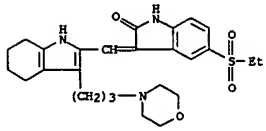
RN 666235-85-4 CAPLUS
CN Piperazine, 1-[3-[2-[[5-(ethylsulfonyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro-1H-indol-3-yl]-1-oxopropyl]-4-methyl- (9CI) (CA INDEX NAME)



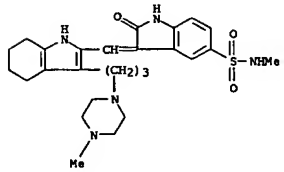
RN 666235-86-5 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N-methyl-2-oxo-3-[[4,5,6,7-tetrahydro-3-[3-(4-morpholinyl)propyl]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)



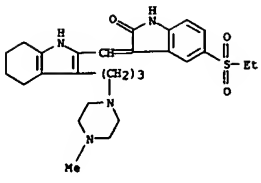
RN 666235-87-6 CAPLUS
CN 2H-Indol-2-one, 5-(ethylsulfonyl)-1,3-dihydro-3-[[4,5,6,7-tetrahydro-3-[3-(4-morpholinyl)propyl]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)



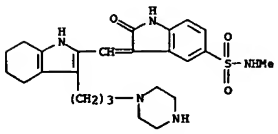
RN 666235-88-7 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N-methyl-2-oxo-3-[[4,5,6,7-tetrahydro-3-[3-(4-methyl-1-piperazinyl)propyl]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)



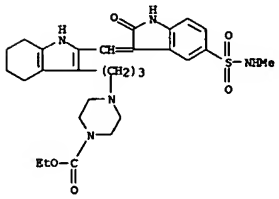
RN 666235-89-8 CAPLUS
CN 2H-Indol-2-one, 5-(ethylsulfonyl)-1,3-dihydro-3-[[4,5,6,7-tetrahydro-3-[3-(4-methyl-1-piperazinyl)propyl]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)



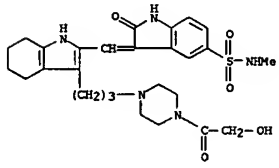
RN 666235-90-1 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N-methyl-2-oxo-3-[[4,5,6,7-tetrahydro-3-[3-(1-piperazinyl)propyl]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)



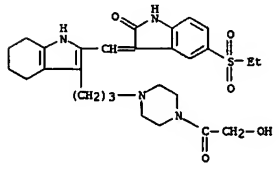
RN 666235-91-2 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[3-[2-[[1,2-dihydro-5-[(methylamino)sulfonyl]-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro-1H-indol-3-yl]propyl]-, ethyl ester (9CI) (CA INDEX NAME)



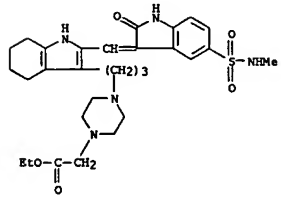
RN 666235-92-3 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[3-[2-[[5-(ethylsulfonyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro-1H-indol-3-yl]propyl]-, ethyl ester (9CI) (CA INDEX NAME)



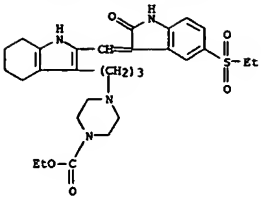
RN 666235-96-7 CAPLUS
CN Piperazine, 1-[3-[2-[[5-(ethylsulfonyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro-1H-indol-3-yl]propyl]-4-(hydroxyacetyl)- (9CI) (CA INDEX NAME)



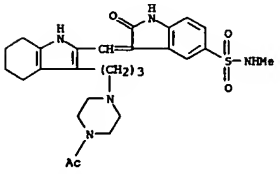
RN 666235-97-8 CAPLUS
CN 1-Piperazineacetic acid, 4-[3-[2-[[1,2-dihydro-5-[(methylamino)sulfonyl]-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro-1H-indol-3-yl]propyl]-, ethyl ester (9CI) (CA INDEX NAME)



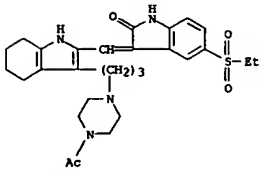
RN 666235-98-9 CAPLUS
CN 1-Piperazineacetic acid, 4-[3-[2-[[1,2-dihydro-5-[(methylamino)sulfonyl]-2-



RN 666235-93-4 CAPLUS
CN Piperazine, 1-acetyl-4-[3-[2-[[1,2-dihydro-5-[(methylamino)sulfonyl]-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro-1H-indol-3-yl]propyl]- (9CI) (CA INDEX NAME)

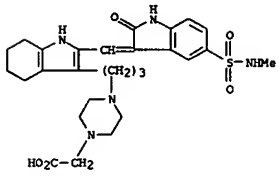


RN 666235-94-5 CAPLUS
CN Piperazine, 1-acetyl-4-[3-[2-[[5-(ethylsulfonyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro-1H-indol-3-yl]propyl]- (9CI) (CA INDEX NAME)

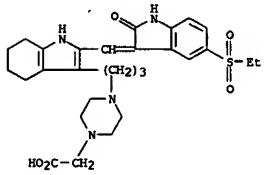


RN 666235-95-6 CAPLUS
CN Piperazine, 1-[3-[2-[[1,2-dihydro-5-[(methylamino)sulfonyl]-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro-1H-indol-3-yl]propyl]-4-(hydroxyacetyl)- (9CI) (CA INDEX NAME)

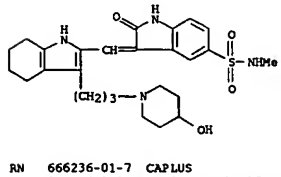
oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro-1H-indol-3-yl]propyl]- (9CI) (CA INDEX NAME)



RN 666235-99-0 CAPLUS
CN 1-Piperazineacetic acid, 4-[3-[2-[[5-(ethylsulfonyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro-1H-indol-3-yl]propyl]- (9CI) (CA INDEX NAME)

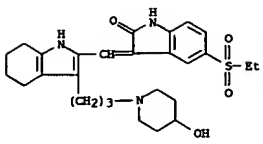


RN 666236-00-6 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N-methyl-2-oxo-3-[[4,5,6,7-tetrahydro-3-[3-(4-hydroxy-1-piperidinyl)propyl]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

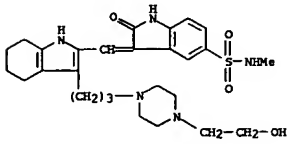


RN 666236-01-7 CAPLUS
CN 2H-Indol-2-one, 5-(ethylsulfonyl)-1,3-dihydro-3-[[4,5,6,7-tetrahydro-3-[3-(4-hydroxy-1-piperidinyl)propyl]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

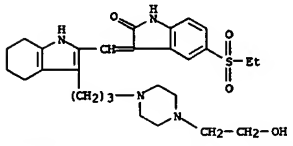
L4 ANSWER 15 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 666236-02-8 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N-methyl-2-oxo-3-[[4,5,6,7-tetrahydro-3-[3-[4-(2-hydroxyethyl)-1-piperazinyl]propyl]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)



RN 666236-03-9 CAPLUS
CN 2H-Indol-2-one, 5-(ethylsulfonyl)-1,3-dihydro-3-[[4,5,6,7-tetrahydro-3-[3-[4-(2-hydroxyethyl)-1-piperazinyl]propyl]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

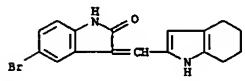


REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 16 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:930718 CAPLUS
DOCUMENT NUMBER: 139:391339
TITLE: Method of determining an efficacious dose of a drug
INVENTOR(S): Fong, Annie; Hirth, Klaus Peter
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 15 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003219380	A1	20031127	US 1998-186475	19981104
PRIORITY APPLN. INFO.:			US 1997-64935P P	19971107

OTHER SOURCE(S): MARPAT 139:391339
AB The present invention relates to a method of determining an efficacious dose of a drug administered to a subject for the purpose of modulating angiogenesis, including conditions manifested by cell proliferation, cell differentiation, or cell survival. The method comprises the step of monitoring a marker related to angiogenesis. The drug used in the present invention is an indolinone compound (Markush structure and individual structures are given). The invention also features a kit for determining the efficacious dose of the drug.
IT 204003-89-4
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method of determining an efficacious dose of a drug)
RN 204003-89-4 CAPLUS
CN 2H-Indol-2-one, 5-bromo-1,3-dihydro-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



L4 ANSWER 17 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:633389 CAPLUS
DOCUMENT NUMBER: 139:159929
TITLE: Non-myeloablative tolerogenic treatment with tyrphostins
INVENTOR(S): Slavin, Shimon; Morecki, Shoshana; Levitzki, Alexander; Gazit, Aviv
PATENT ASSIGNEE(S): Yissum Research Development Company of the Hebrew University of Jerusalem, Israel; Hadasit Medical Research Services and Development Ltd.
SOURCE: PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003065971	A2	20030814	WO 2002-IL467	20020616
WO 2003065971	C2	20031120		
WO 2003065971	A3	20040916		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2450807	AA	20030814	CA 2002-2450807	20020616
EP 1482983	A2	20041208	EP 2002-738590	20020616
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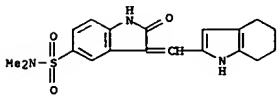
JP 2005516983	T2	20050609	JP 2003-565397	20020616
US 2004197335	A1	20041007	US 2003-479523	20031211
PRIORITY APPLN. INFO.:			US 2001-297795P P	20010614
			WO 2002-IL467 W	20020616

AB A method of inducing immune tolerance in a first mammal to antigens of a second, non-syngeneic, mammal, is disclosed. The method is utilized to minimize graft rejection and/or reduce graft-vs.-host diseases in transplantation procedures and to produce hematopoietic mixed chimeras. Methods of determining the activity of tyrphostins and the optimal concentration thereof in this method are also disclosed.
IT 330161-87-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(non-myeloablative tolerogenic treatment with tyrphostins to eliminate lymphocyte responding to non-syngeneic donor antigens)
RN 330161-87-0 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N,N-dimethyl-2-oxo-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)

L4 ANSWER 17 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



L4 ANSWER 18 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:221660 CAPLUS
DOCUMENT NUMBER: 138:238009
TITLE: Preparation of 3-(4,5,6,7-tetrahydroindol-2-ylmethylidene)-2-indolinones as kinase inhibitors for treatment of cancer
INVENTOR(S): Liang, Congxin; Guan, Huiping; Tang, Peng Cho; Blake, Robert A.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003022815	A1	20030320	WO 2002-US25974	20020910
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2459879	AA	20030320	CA 2002-2459879	20020910
US 2003119819	A1	20030626	US 2002-238051	20020910
US 6777417	B2	20040817		
EP 1436259	A1	20040714	EP 2002-780264	20020910
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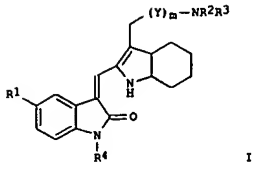
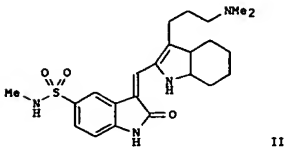
BR 2002012435	A	20040817	BR 2002-12435	20020910
JP 2005506982	T2	20050310	JP 2003-526891	20020910
US 2004266855	A1	20041230	US 2004-889050	20040713
PRIORITY APPLN. INFO.:			US 2001-318508P	P 20010910
			US 2002-238051	A3 20020910
			WO 2002-US25974	W 20020910

OTHER SOURCE(S): MARPAT 138:238009
GI

L4 ANSWER 18 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



I



II

AB Title compds. I [wherein Y = CH2, CH2CH2, CO, or COCH2; m = 0-1; R1 = SOnR5 or SO2NR6R7; R2 = H or (hydroxy)alkyl; R3 = (hydroxy)alkyl; or NR2R3 = heterocyclyl; R4 = H, PO(OR8)2, COR9, CHR10NR11R12; n = 0-2; R5 = (ar)alkyl; R6 and R7 = independently H, (cyclo)alkyl, alkoxyalkyl, or hydroxyalkyl; R8 = independently H or alkyl; R9 = alkyl; R10 = H or alkyl; R11 and R12 = independently H or alkyl; or NR11R12 = heterocyclyl; and pharmaceutically acceptable salts thereof] were prepared For example, cyclocondensation of 5-aminolevulinic acid·HCl with 1,2-cyclohexanedione gave 3-(4-oxo-4,5,6,7-tetrahydro-1H-indol-3-yl)propionic acid (67%). Amidation with NHMe2 (60%), reduction to the amine (90%), and reaction with POCl3 and DMF afforded 3-(3-dimethylaminopropyl)-4,5,6,7-tetrahydro-1H-indole-2-carbaldehyde (50%). Condensation of the aldehyde with 5-methylaminosulfonyloxindole in the presence of piperidine in EtOH provided (Z)-II (70%). I inhibit Src kinase activity and are useful for the treatment of Src kinase related disorders, such as cancer (no data).

IT **502156-90-3P**, (Z)-3-[1-[3-(3-Dimethylaminopropyl)-4,5,6,7-tetrahydro-1H-indol-2-yl]methylidene]-2-oxo-2,3-dihydro-1H-indole-5-sulfonic acid methylamide **502156-91-4P**, (Z)-3-[1-[3-[3-(4-Methylpiperazin-1-yl)propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylidene]-2-oxo-2,3-dihydro-1H-indole-5-sulfonic acid methylamide **502156-92-5P**, (Z)-3-[1-[3-[3-(3,5-Dimethylpiperazin-1-yl)-3-oxopropyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylidene]-2-oxo-2,3-dihydro-1H-indole-5-sulfonic acid methylamide **502156-94-7P**, (Z)-3-[1-[3-[3-(4-Methylpiperazin-1-yl)-3-oxopropyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylidene]-2-oxo-2,3-dihydro-1H-indole-5-sulfonic acid methylamide **502156-96-9P**, (Z)-3-[1-[3-[3-(3,5-Dimethylpiperazin-1-yl)-3-oxopropyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylidene]-5-ethanesulfonyl-1,3-dihydroindol-2-one **502156-98-1P**, (Z)-5-Ethanesulfonyl-3-[1-[3-[3-(4-methylpiperazin-1-yl)-3-oxopropyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylidene]-1,3-dihydroindol-2-one **502157-00-8P**, (Z)-4-[3-[2-[(5-Methylsulfamoyl-2-oxo-1,2-

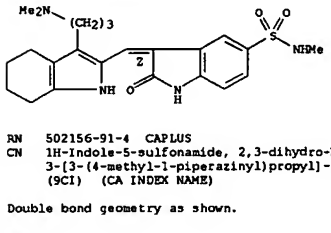
L4 ANSWER 18 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

dihydroindol-3-ylidene)methyl]-4,5,6,7-tetrahydro-1H-indol-3-yl]propyl]piperazine-1-carboxylic acid ethyl ester **502157-06-4P**, (Z)-4-[3-[2-[(5-Ethanesulfonyl-2-oxo-1,2-dihydroindol-3-ylidene)methyl]-4,5,6,7-tetrahydro-1H-indol-3-yl]propyl]piperazine-1-carboxylic acid ethyl ester **502157-07-5P**, (Z)-3-[1-[3-[3-(4-Acetylpiperazin-1-yl)propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylidene]-2-oxo-2,3-dihydro-1H-indole-5-sulfonic acid methylamide **502157-08-6P**, (Z)-3-[1-[3-[3-(4-Acetylpiperazin-1-yl)propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylidene]-5-ethanesulfonyl-1,3-dihydroindol-2-one **502157-10-0P**, (Z)-3-[1-[3-[3-(4-Formylpiperazin-1-yl)propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylidene]-2-oxo-2,3-dihydro-1H-indole-5-sulfonic acid methylamide **502157-11-1P**, (Z)-3-[1-[3-[3-[4-(2-Hydroxyacetyl)piperazin-1-yl]propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylidene]-2-oxo-2,3-dihydro-1H-indole-5-sulfonic acid methylamide **502157-13-3P**, (Z)-5-Ethanesulfonyl-3-[1-[3-[3-[4-(2-hydroxyacetyl)piperazin-1-yl]propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylidene]-1,3-dihydroindol-2-one **502157-14-4P**, (Z)-2-Oxo-3-[1-[3-[3-(piperazin-1-yl)propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylidene]-2,3-dihydro-1H-indole-5-sulfonic acid methylamide **502157-15-5P**, (Z)-4-[3-[2-[(5-Ethanesulfonyl-2-oxo-1,2-dihydroindol-3-ylidene)methyl]-4,5,6,7-tetrahydro-1H-indol-3-yl]propyl]piperazine-1-carboxaldehyde **502157-16-6P**, (Z)-[4-[3-[2-[(5-Methylsulfamoyl-2-oxo-1,2-dihydroindol-3-ylidene)methyl]-4,5,6,7-tetrahydro-1H-indol-3-yl]propyl]piperazin-1-yl]acetic acid ethyl ester **502157-18-8P**, (Z)-[4-[3-[2-[(5-Methylsulfamoyl-2-oxo-1,2-dihydroindol-3-ylidene)methyl]-4,5,6,7-tetrahydro-1H-indol-3-yl]propyl]piperazin-1-yl]acetic acid **502157-19-9P**, (Z)-[4-[3-[2-[(5-Ethanesulfonyl-2-oxo-1,2-dihydroindol-3-ylidene)methyl]-4,5,6,7-tetrahydro-1H-indol-3-yl]propyl]piperazin-1-yl]acetic acid **502157-21-3P**, (Z)-3-[1-[3-[3-(4-Hydroxypiperidin-1-yl)propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylidene]-2-oxo-2,3-dihydro-1H-indole-5-sulfonic acid methylamide **502157-22-4P**, (Z)-5-Ethanesulfonyl-3-[1-[3-[3-(4-hydroxypiperidin-1-yl)propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylidene]-1,3-dihydroindol-2-one **502157-24-6P**, (Z)-3-[1-[3-[3-[4-(2-Hydroxyethyl)piperazin-1-yl]propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylidene]-2-oxo-2,3-dihydro-1H-indole-5-sulfonic acid methylamide **502157-26-8P**, (Z)-5-Ethanesulfonyl-3-[1-[3-[3-[4-(2-hydroxyethyl)piperazin-1-yl]propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylidene]-1,3-dihydroindol-2-one **502157-28-0P**, (Z)-3-[1-[3-[3-(3,5-Dimethylpiperazin-1-yl)propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylidene]-2-oxo-2,3-dihydro-1H-indole-5-sulfonic acid methylamide **502157-29-1P**, (Z)-3-[1-[3-[3-(3,5-Dimethylpiperazin-1-yl)propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylidene]-5-ethanesulfonyl-1,3-dihydroindol-2-one **502157-31-5P**, (Z)-3-[1-[3-[3-(Morpholin-4-yl)propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylidene]-2-oxo-2,3-dihydro-1H-indole-5-sulfonic acid (2-hydroxyethyl)amide **502157-32-6P**, (Z)-3-[1-[3-(3-Dimethylaminopropyl)-4,5,6,7-tetrahydro-1H-indol-2-yl]methylidene]-2-oxo-2,3-dihydro-1H-indole-5-sulfonic acid (2-hydroxyethyl)amide **502157-33-7P**, (Z)-3-[1-[3-[3-[(2-Hydroxyethyl)methylamino]propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylidene]-2-oxo-2,3-dihydro-1H-indole-5-sulfonic acid methylamide **502157-36-0P**, (Z)-5-Ethanesulfonyl-3-[1-[3-[3-[(2-hydroxyethyl)methylamino]propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylidene]-1,3-dihydroindol-2-one
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Src kinase inhibitor; prepn. of (indolylmethylidene)indolinone Src kinase inhibitors by condensation of indolecarboxaldehydes with indolinones for treatment of cancer)

L4 ANSWER 18 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

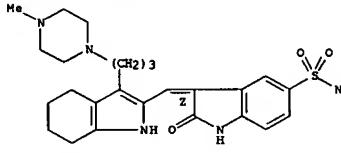
RN 502156-90-3 CAPLUS
CN 1H-Indole-5-sulfonamide, 3-[[3-[3-(dimethylamino)propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylene]-2,3-dihydro-N-methyl-2-oxo-, (3Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.



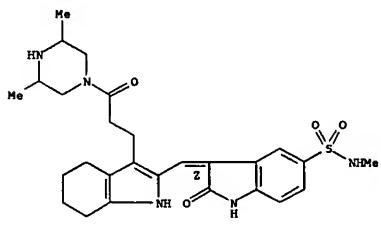
RN 502156-91-4 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N-methyl-2-oxo-3-[[4,5,6,7-tetrahydro-3-[3-(4-methyl-1-piperazinyl)propyl]-1H-indol-2-yl]methylene]-, (3Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.



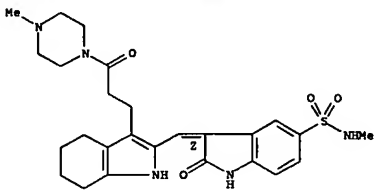
RN 502156-92-5 CAPLUS
CN Piperazine, 1-[3-[2-[(Z)-[1,2-dihydro-5-[(methylamino)sulfonyl]-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro-1H-indol-3-yl]-1-oxopropyl]-3,5-dimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



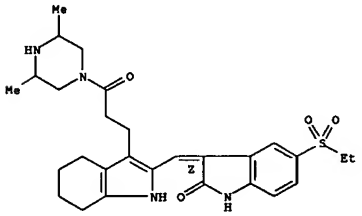
RN 502156-94-7 CAPLUS
CN Piperazine, 1-[3-[2-[(Z)-[1,2-dihydro-5-[(methylamino)sulfonyl]-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro-1H-indol-3-yl]-1-oxopropyl]-4-methyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



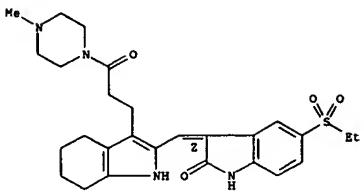
RN 502156-96-9 CAPLUS
CN Piperazine, 1-[3-[2-[(Z)-[5-(ethylsulfonyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro-1H-indol-3-yl]-1-oxopropyl]-3,5-dimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



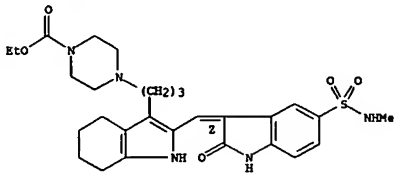
RN 502156-98-1 CAPLUS
CN Piperazine, 1-[3-[2-[(Z)-[5-(ethylsulfonyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro-1H-indol-3-yl]-1-oxopropyl]-4-methyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



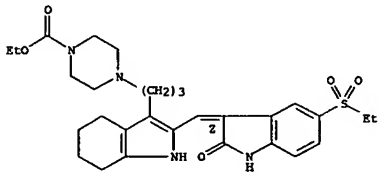
RN 502157-00-8 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[3-[2-[(Z)-[1,2-dihydro-5-[(methylamino)sulfonyl]-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro-1H-indol-3-yl]propyl]-, ethyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 502157-06-4 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[3-[2-[(Z)-[5-(ethylsulfonyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro-1H-indol-3-yl]propyl]-, ethyl ester (9CI) (CA INDEX NAME)

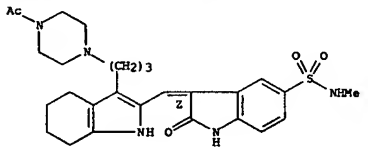
Double bond geometry as shown.



RN 502157-07-5 CAPLUS
CN Piperazine, 1-acetyl-4-[3-[2-[(Z)-[1,2-dihydro-5-[(methylamino)sulfonyl]-2-

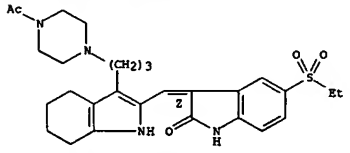
oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro-1H-indol-3-yl]propyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



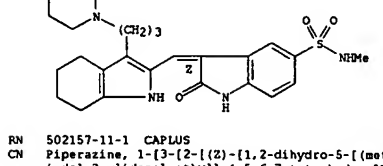
RN 502157-08-6 CAPLUS
CN Piperazine, 1-acetyl-4-[3-[2-[(Z)-[5-(ethylsulfonyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro-1H-indol-3-yl]propyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



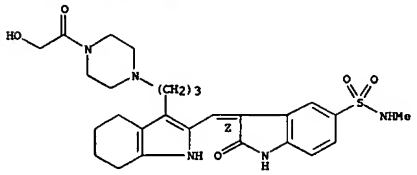
RN 502157-10-0 CAPLUS
CN 1H-Indole-5-sulfonamide, 3-[[3-[3-(4-formyl-1-piperazinyl)propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylene]-2,3-dihydro-N-methyl-2-oxo-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



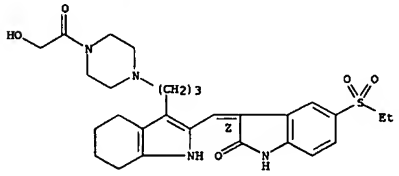
RN 502157-11-1 CAPLUS
CN Piperazine, 1-[3-[2-[(Z)-[1,2-dihydro-5-[(methylamino)sulfonyl]-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro-1H-indol-3-yl]propyl]-4-(hydroxyacetyl)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



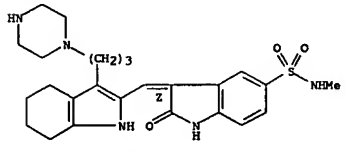
RN 502157-13-3 CAPLUS
CN Piperazine, 1-[3-[2-[(Z)-[5-(ethylsulfonyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro-1H-indol-3-yl]propyl]-4-(hydroxyacetyl)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



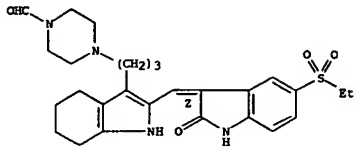
RN 502157-14-4 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N-methyl-2-oxo-3-[[4,5,6,7-tetrahydro-3-[3-(1-piperazinyl)propyl]-1H-indol-2-yl]methylene]-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



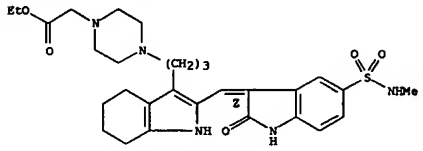
RN 502157-15-5 CAPLUS
CN 1-Piperazinecarboxaldehyde, 4-[3-[2-[(Z)-[5-(ethylsulfonyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro-1H-indol-3-yl]propyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



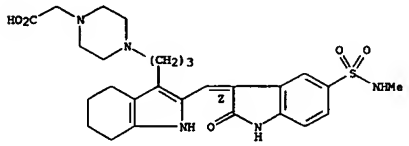
RN 502157-16-6 CAPLUS
CN 1-Piperazineacetic acid, 4-[3-[2-[(Z)-[1,2-dihydro-5-[(methylamino)sulfonyl]-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro-1H-indol-3-yl]propyl]-, ethyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.



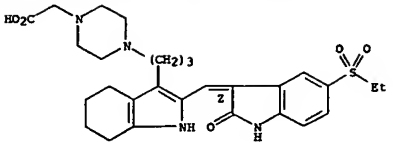
RN 502157-18-8 CAPLUS
CN 1-Piperazineacetic acid, 4-[3-[2-[(Z)-[1,2-dihydro-5-[(methylamino)sulfonyl]-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro-1H-indol-3-yl]propyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



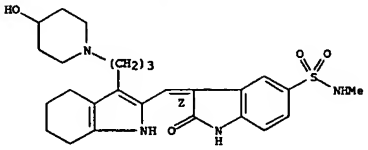
RN 502157-19-9 CAPLUS
CN 1-Piperazineacetic acid, 4-[3-[2-[(Z)-[5-(ethylsulfonyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro-1H-indol-3-yl]propyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



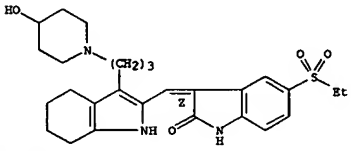
RN 502157-21-3 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N-methyl-2-oxo-3-[[4,5,6,7-tetrahydro-3-[3-(4-hydroxy-1-piperidinyl)propyl]-1H-indol-2-yl]methylene]-, (3Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.



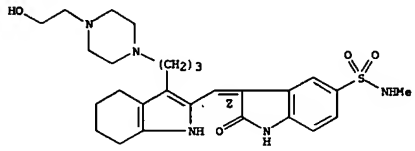
RN 502157-22-4 CAPLUS
CN 2H-Indol-2-one, 5-(ethylsulfonyl)-1,3-dihydro-3-[[4,5,6,7-tetrahydro-3-[3-(4-hydroxy-1-piperidinyl)propyl]-1H-indol-2-yl]methylene]-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



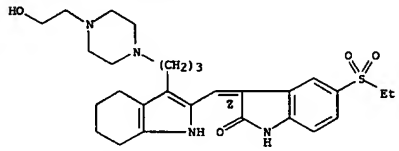
RN 502157-24-6 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N-methyl-2-oxo-3-[[4,5,6,7-tetrahydro-3-[3-[4-(2-hydroxyethyl)-1-piperazinyl]propyl]-1H-indol-2-yl]methylene]-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



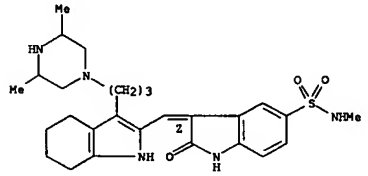
RN 502157-26-8 CAPLUS
CN 2H-Indol-2-one, 5-(ethylsulfonyl)-1,3-dihydro-3-[[4,5,6,7-tetrahydro-3-[3-[4-(2-hydroxyethyl)-1-piperazinyl]propyl]-1H-indol-2-yl]methylene]-, (3Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.



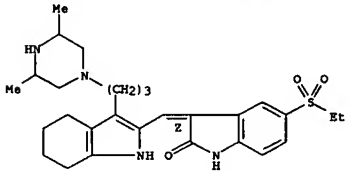
RN 502157-28-0 CAPLUS
CN 1H-Indole-5-sulfonamide, 3-[[3-[3-(3,5-dimethyl-1-piperazinyl)propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylene]-2,3-dihydro-N-methyl-2-oxo-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



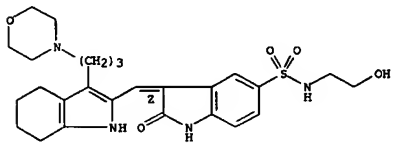
RN 502157-29-1 CAPLUS
CN 2H-Indol-2-one, 3-[[3-[3-(3,5-dimethyl-1-piperazinyl)propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylene]-5-(ethylsulfonyl)-1,3-dihydro-, (3Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.



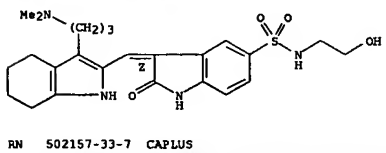
RN 502157-31-5 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N-(2-hydroxyethyl)-2-oxo-3-[[4,5,6,7-tetrahydro-3-[3-(4-morpholinyl)propyl]-1H-indol-2-yl]methylene]-, (3Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 502157-32-6 CAPLUS
CN 1H-Indole-5-sulfonamide, 3-[[3-[3-(dimethylamino)propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylene]-2,3-dihydro-N-(2-hydroxyethyl)-2-oxo-, (3Z)- (9CI) (CA INDEX NAME)

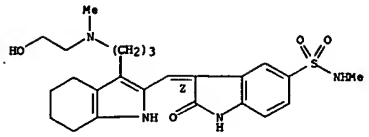
Double bond geometry as shown.



RN 502157-33-7 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N-methyl-2-oxo-3-[[4,5,6,7-tetrahydro-3-[3-[(2-hydroxyethyl)methylamino]propyl]-1H-indol-2-yl]methylene]-, (3Z)-(9CI) (CA INDEX NAME)

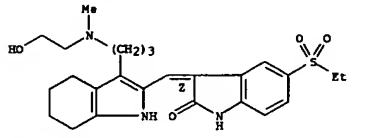
Double bond geometry as shown.

L4 ANSWER 18 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 502157-36-0 CAPLUS
CN 2H-Indol-2-one, 5-(ethylsulfonyl)-1,3-dihydro-3-[[4,5,6,7-tetrahydro-3-[3-[(2-hydroxyethyl)methylamino]propyl]-1H-indol-2-yl]methylene]-, (3Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 19 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

REFERENCE COUNT: 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

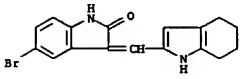
L4 ANSWER 19 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:628660 CAPLUS
DOCUMENT NUMBER: 137:346843
TITLE: Effects of vascular endothelial and platelet-derived growth factor receptor inhibitors on long-term cultures from normal human bone marrow
AUTHOR(S): Duhrsen, Ulrich; Martinez, Tanja; Vohwinkel, Gabi; Ergun, Suleyman; Sun, Li; McMahon, Gerald; Durig, Jan; Hossfeld, Dieter Kurt; Fiedler, Walter
CORPORATE SOURCE: Zentrum fur Innere Medizin, Abteilung fur Hamatologie, Universitatsklinikum Essen, Germany
SOURCE: Growth Factors (2001), 19(1), 1-17
CODEN: GRFAEC; ISSN: 0897-7194
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Endothelial cells and fibroblasts are important constituents of the hemopoietic microenvironment. Growth and function of these cells are controlled by a variety of cytokines, including VEGF and PDGF. The authors analyzed the effects of novel tyrosine kinase inhibitors targeting the VEGF and PDGF receptors (compds. SU5614 and SU5768) on the performance of long-term cultures from normal human bone marrow. In developing cultures, the inhibitors induced a dose-dependent reduction in stromal fibroblasts, macrophages and endothelial cells with a concomitant decrease in blood cell production and an increase in fat cells. For SU5614, the concentration inhibiting stroma formation by 50% (IC50) was 123 nM, and the IC50 for hemopoietic colony forming cell output was 186 nM. For SU5768, the resp. values were 871 nM and 331 nM. Changes in stroma composition and inhibition of hemopoietic cell production were also demonstrable after delayed addition of the inhibitors to established cultures. By contrast, hemopoietic colony formation in clonogenic agar cultures was unimpaired (IC50 not reached at 100 μM). Immunofluorescence studies and time course analyses suggested that the primary effect of the inhibitors was interference with the proliferation and function of fibroblasts and endothelial cells which in turn resulted in decreased hemopoiesis and increased adipogenesis. This was associated with decreased levels in conditioned media of granulocyte-macrophage colony-stimulating factor, interleukin-6 and leptin. VEGF and PDGF may play a hitherto underestimated role in the control of blood cell formation. VEGF/PDGF receptor inhibitors may have therapeutic potential in stroma diseases such as myelofibrosis. Since they weaken the stimulatory signals provided by the microenvironment, they may also be of value in the treatment of leukemia and other neoplastic bone marrow diseases.

IT 204003-89-4, SU 5768
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(PDGF and VEGF inhibitors biochem. and cellular characterization using bone marrow endothelial cells and fibroblasts)

RN 204003-89-4 CAPLUS
CN 2H-Indol-2-one, 5-bromo-1,3-dihydro-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



L4 ANSWER 20 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:539677 CAPLUS
DOCUMENT NUMBER: 137:109202
TITLE: Preparation of 4-aryl substituted indolinones as protein kinase signal transduction modulators for inhibiting abnormal cell proliferation
INVENTOR(S): Cui, Jingrong; Zhang, Ruofei; Shen, Hong; Chu, Ji Yu; Zhang, Fang-Jie; Koenig, Marcel; Do, Steven Huy; Li, Xiaoyuan; Wei, Chung Chen; Tang, Peng Cho
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 560 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002055517	A2	20020718	WO 2001-US48564	20011220
WO 2002055517	A3	20020926		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2432114	AA	20020718	CA 2001-2432114	20011220
US 2003069297	A1	20030410	US 2001-23488	20011220
US 6677368	B2	20040113		
EP 1349852	A2	20031008	EP 2001-997065	20011220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004518669	T2	20040624	JP 2002-556186	20011220
US 2004157909	A1	20040812	US 2003-736243	20031216
US 6861418	B2	20050301		

PRIORITY APPLN. INFO.: US 2000-256479P P 20001220
US 2001-23488 A3 20011220
WO 2001-US48564 W 20011220

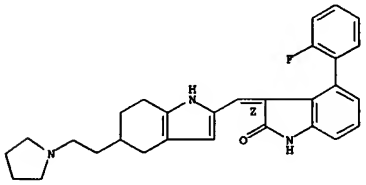
OTHER SOURCE(S): MARPAT 137:109202
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [R1 = (un)substituted aryl or heteroaryl; R2 = H, halo, alkyl, alkenyl, alkynyl, heterocyclyl, etc.; R3 = (un)substituted pyrrole or cycloalkenylpyrrole], as well as pharmaceutical compns. thereof, are prepared and disclosed as compds. capable of modulating protein kinase signal transduction in order to regulate, modulate and/or inhibit abnormal cell proliferation. Thus II, was prepared via condensation of 4-phenyl-1,3-dihydroindol-2-one with 5-formyl-2-methyl-4-[3-(4-methylpiperazin-1-yl)propyl]-1H-pyrrole-3-carboxylic acid Et ester. I were evaluated against eight specfic kinases, e.g., FGFR1, for which I possessed IC50 values (μM) of 0.0091-2.07. The present invention also

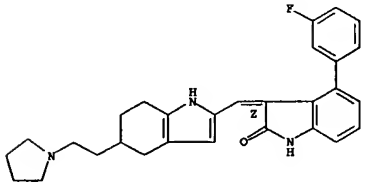
L4 ANSWER 20 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
relates to methods for treating protein kinase related disorders.
IT 442559-47-9P 442559-48-0P 442559-49-1P
442559-50-4P 442559-51-5P 442559-52-6P
442560-33-0P 442560-34-1P 442560-35-2P
442560-36-3P 442560-37-4P 442561-22-0P
442561-23-1P 442561-24-2P 442562-17-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of (aryl)(pyrrolylmethylene)indolinones as protein kinase signal transduction modulators)
RN 442559-47-9 CAPLUS
CN 2H-Indol-2-one, 4-(2-fluorophenyl)-1,3-dihydro-3-[[4,5,6,7-tetrahydro-5-[2-(1-pyrrolidinyl)ethyl]-1H-indol-2-yl]methylene]-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



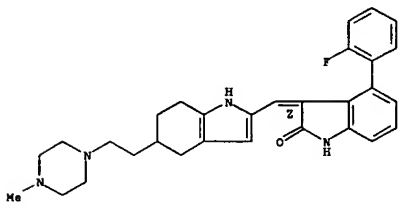
RN 442559-48-0 CAPLUS
CN 2H-Indol-2-one, 4-(3-fluorophenyl)-1,3-dihydro-3-[[4,5,6,7-tetrahydro-5-[2-(1-pyrrolidinyl)ethyl]-1H-indol-2-yl]methylene]-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



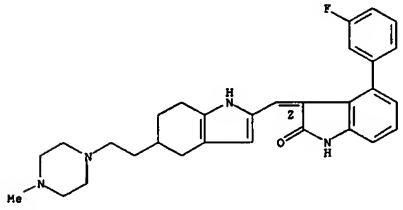
RN 442559-49-1 CAPLUS
CN 2H-Indol-2-one, 4-(2-fluorophenyl)-1,3-dihydro-3-[[4,5,6,7-tetrahydro-5-[2-(4-morpholinyl)ethyl]-1H-indol-2-yl]methylene]-, (3Z)- (9CI) (CA INDEX NAME)

L4 ANSWER 20 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 442559-52-6 CAPLUS
CN 2H-Indol-2-one, 4-(3-fluorophenyl)-1,3-dihydro-3-[[4,5,6,7-tetrahydro-5-[2-(4-methyl-1-piperazinyl)ethyl]-1H-indol-2-yl]methylene]-, (3Z)- (9CI) (CA INDEX NAME)

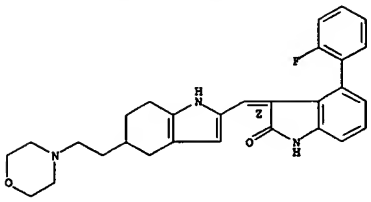
Double bond geometry as shown.



RN 442560-33-0 CAPLUS
CN 2H-Indol-2-one, 3-[[3-[3-(dimethylamino)propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylene]-4-(4-fluorophenyl)-1,3-dihydro-, (3Z)- (9CI) (CA INDEX NAME)

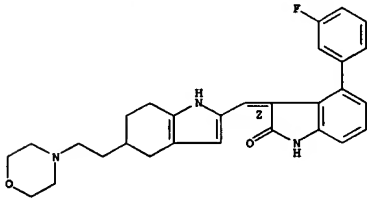
Double bond geometry as shown.

L4 ANSWER 20 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
Double bond geometry as shown.



RN 442559-50-4 CAPLUS
CN 2H-Indol-2-one, 4-(3-fluorophenyl)-1,3-dihydro-3-[[4,5,6,7-tetrahydro-5-[2-(4-morpholinyl)ethyl]-1H-indol-2-yl]methylene]-, (3Z)- (9CI) (CA INDEX NAME)

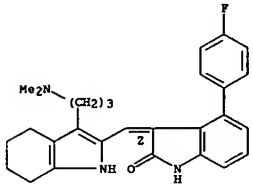
Double bond geometry as shown.



RN 442559-51-5 CAPLUS
CN 2H-Indol-2-one, 4-(2-fluorophenyl)-1,3-dihydro-3-[[4,5,6,7-tetrahydro-5-[2-(4-methyl-1-piperazinyl)ethyl]-1H-indol-2-yl]methylene]-, (3Z)- (9CI) (CA INDEX NAME)

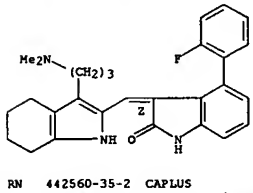
Double bond geometry as shown.

L4 ANSWER 20 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



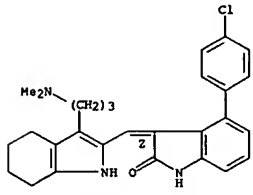
RN 442560-34-1 CAPLUS
CN 2H-Indol-2-one, 3-[[3-[3-(dimethylamino)propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylene]-4-(2-fluorophenyl)-1,3-dihydro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 442560-35-2 CAPLUS
CN 2H-Indol-2-one, 4-(4-chlorophenyl)-3-[[3-[3-(dimethylamino)propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylene]-1,3-dihydro-, (3Z)- (9CI) (CA INDEX NAME)

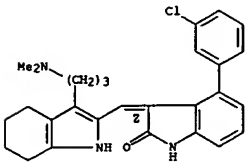
Double bond geometry as shown.



RN 442560-36-3 CAPLUS
CN 2H-Indol-2-one, 4-(3-chlorophenyl)-3-[[3-[3-(dimethylamino)propyl]-4,5,6,7-

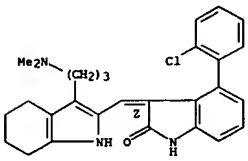
L4 ANSWER 20 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
tetrahydro-1H-indol-2-yl]methylene]-1,3-dihydro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



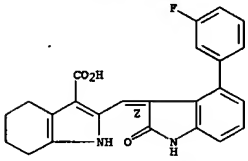
RN 442560-37-4 CAPLUS
CN 2H-Indol-2-one, 4-(2-chlorophenyl)-3-[[3-[3-(dimethylamino)propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylene]-1,3-dihydro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



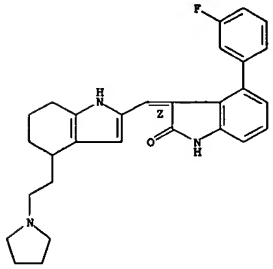
RN 442561-22-0 CAPLUS
CN 1H-Indole-3-carboxylic acid, 2-[(Z)-[4-(3-fluorophenyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



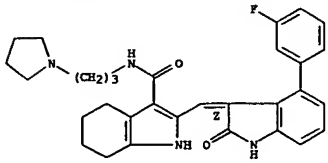
RN 442561-23-1 CAPLUS
CN 1H-Indole-3-carboxamide, 2-[(Z)-[4-(3-fluorophenyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro-N-[3-(1-pyrrolidinyl)propyl]-

L4 ANSWER 20 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



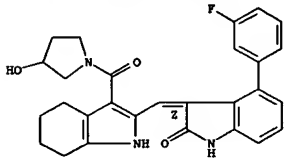
L4 ANSWER 20 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
(9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 442561-24-2 CAPLUS
CN 3-Pyrrolidinol, 1-[[2-[(Z)-[4-(3-fluorophenyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro-1H-indol-3-yl]carbonyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 442562-17-6 CAPLUS
CN 2H-Indol-2-one, 4-(3-fluorophenyl)-1,3-dihydro-3-[[4,5,6,7-tetrahydro-4-[2-(1-pyrrolidinyl)ethyl]-1H-indol-2-yl]methylene]-, (3Z)- (9CI) (CA INDEX NAME)

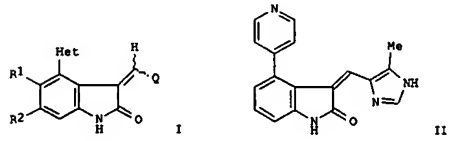
Double bond geometry as shown.

L4 ANSWER 21 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	2002:31440 CAPLUS
DOCUMENT NUMBER:	136:102386
TITLE:	Preparation and use of 4-heteroacyl-3-heteroarylidenyl-2-indolinones and their use as protein kinase inhibitors
INVENTOR(S):	Tang, Peng Cho; Wei, Chung Chen; Huang, Ping; Cui, Jingron
PATENT ASSIGNEE(S):	Sugen, Inc., USA
SOURCE:	PCT Int. Appl., 164 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002002551	A1	20020110	WO 2001-US20768	20010629
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2414468	AA	20020110	CA 2001-2414468	20010629
US 2002187978	A1	20021212	US 2001-894902	20010629
US 6635640	B2	20031021		
EP 1296975	A1	20030402	EP 2001-948830	20010629
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004502686	T2	20040129	JP 2002-507803	20010629
US 2004097497	A1	20040520	US 2003-648810	20030827
PRIORITY APPLN. INFO.:			US 2000-215654P	P 20000630
			US 2001-894902	A3 20010629
			WO 2001-US20768	W 20010629

OTHER SOURCE(S): MARPAT 136:102386
GI

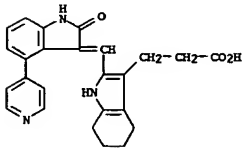


AB Title compds. I [R1-2 = H, alkyl, cycloalkyl, aryl, heteroaryl, heteroalicyclic, halo, etc.; Het = (un)substituted aromatic heterocycle containing at least one and not more than two N atoms, tetrahydro(thio)pyranyl, (thio)morpholino, piperidinyl, piperazinyl, tetrazolyl, etc.; Q = (un)substituted aromatic heterocycle containing not more

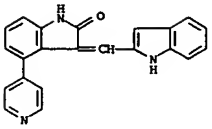
than two N atoms, 5-membered ring (un)substituted heterocycle contg. N, O or S, e.g., imidazolyl, pyrrolyl, indolyl, etc.] with some exceptions, were prepd. Included are 75 synthetic examples and results for several protein tyrosine kinase assays for those compds. For instance, 4-bromoindole was coupled to bis(pinacolato)diborane (DMSO, KOAc, PdCl2(dppf)-CH2Cl2, 80°C, 22 h). The resulting dioxaborolane was coupled to 4-bromopyridine-HCl (THF, Pd(PPh3)4, NaOH, 70°C, 6 h) to give the indole which was treated with C5H5N-Br3 (t-BuOH/EtOH/H2O, 1h) followed by zinc (stirred 1 addnl. hour) to give 4-(pyridin-4-yl)-1,3-dyhydroindol-2-one as a yellow solid. Condensation of this intermediate with 5-methylimidazole-4-carboxaldehyde (EtOH, piperidine, 2 days) afforded II. II had IC50 = 4.88 mM for FGFR-1 tyrosine kinase and 0.03 mM for cdk2/cyclin A tyrosine kinase. I are useful in treating cancer, immunol. disorders, etc.

IT **388116-50-5P 388116-57-2P**, 3-(1H-Indol-2-ylmethylene)-4-(pyridin-4-yl)-1,3-dihydroindol-2-one **388116-58-3P**, 4-(Pyridin-4-yl)-3-(4,5,6,7-tetrahydro-1H-indol-2-ylmethylene)-1,3-dihydroindol-2-one **388116-59-4P**, 3-[5-(2-(Morpholin-4-yl)ethoxy)-1H-indol-2-ylmethylene]-4-(pyridin-4-yl)-1,3-dihydroindol-2-one **388116-62-9P 388116-87-8P 388116-93-6P**, 3-(1H-Indol-2-ylmethylene)-4-(piperidin-4-yl)-1,3-dihydroindol-2-one **388116-94-7P**, 4-(Piperidin-4-yl)-3-(4,5,6,7-tetrahydro-1H-indol-2-ylmethylene)-1,3-dihydroindol-2-one **388116-95-8P**, 3-[5-(2-(Morpholin-4-yl)ethoxy)-1H-indol-2-ylmethylene]-4-(piperidin-4-yl)-1,3-dihydroindol-2-one **388116-98-1P**, 3-[3-(3-Morpholin-4-ylpropyl)-4,5,6,7-tetrahydro-1H-indol-2-ylmethylene]-4-(piperidin-4-yl)-1,3-dihydroindol-2-one
RL: FAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug; preparation and use of 4-heteroaryl-3-heteroarylidenyl-2-indolinones and their use as protein kinase inhibitors)

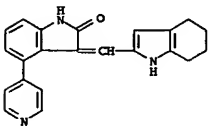
RN 388116-50-5 CAPLUS
CN 1H-Indole-3-propanoic acid, 2-[[1,2-dihydro-2-oxo-4-(4-pyridinyl)-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)



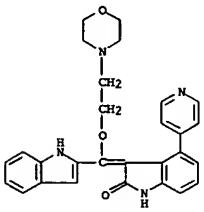
RN 388116-57-2 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-3-(1H-indol-2-ylmethylene)-4-(4-pyridinyl)-(9CI) (CA INDEX NAME)



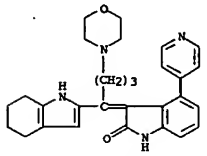
RN 388116-58-3 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-4-(4-pyridinyl)-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



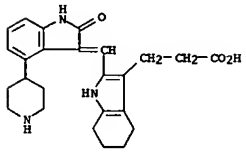
RN 388116-59-4 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-3-[1H-indol-2-yl[2-(4-morpholinyl)ethoxy]methylene]-4-(4-pyridinyl)- (9CI) (CA INDEX NAME)



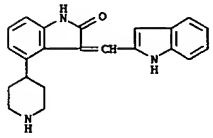
RN 388116-62-9 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-3-[4-(4-morpholinyl)-1-(4,5,6,7-tetrahydro-1H-indol-2-yl)butylidene]-4-(4-pyridinyl)- (9CI) (CA INDEX NAME)



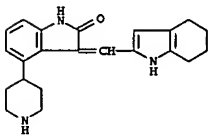
RN 388116-87-8 CAPLUS
CN 1H-Indole-3-propanoic acid, 2-[[1,2-dihydro-2-oxo-4-(4-piperidinyl)-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)



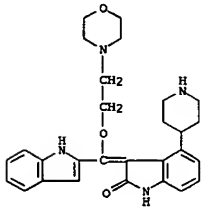
RN 388116-93-6 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-3-(1H-indol-2-ylmethylene)-4-(4-piperidinyl)-(9CI) (CA INDEX NAME)



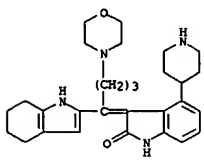
RN 388116-94-7 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-4-(4-piperidinyl)-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



RN 388116-95-8 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-3-[1H-indol-2-yl[2-(4-morpholinyl)ethoxy]methylene]-4-(4-piperidinyl)- (9CI) (CA INDEX NAME)



RN 388116-98-1 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-3-[4-(4-morpholinyl)-1-(4,5,6,7-tetrahydro-1H-indol-2-yl)butylidene]-4-(4-piperidinyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 22 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN

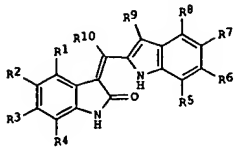
ACCESSION NUMBER: 2001:904107 CAPLUS
DOCUMENT NUMBER: 136:37505
TITLE: Preparation of 3-(2-indolylmethylene)-2-indolinones as protein kinase/phosphatase inhibitors for treatment of proliferative diseases
INVENTOR(S): Tang, Peng Cho; Harris, G. Davis; Li, Xiaoyuan
PATENT ASSIGNEE(S): Sugen, Inc., USA
SOURCE: PCT Int. Appl., 199 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001094312	A2	20011213	WO 2001-US17961	20010604
WO 2001094312	A3	20020808		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2410509	AA	20011213	CA 2001-2410509	20010604
US 2002052369	A1	20020502	US 2001-871700	20010604
US 6706709	B2	20040316		
EP 1294688	A2	20030326	EP 2001-946059	20010604
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003535847	T2	20031202	JP 2002-501862	20010604
US 2004147586	A1	20040729	US 2003-725277	20031202

PRIORITY APPLN. INFO.: US 2000-209162P P 20000602
US 2001-871700 A3 20010604
WO 2001-US17961 W 20010604

OTHER SOURCE(S): MARPAT 136:37505
GI

L4 ANSWER 22 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



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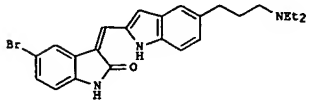


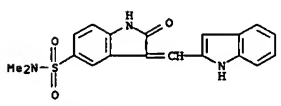
II

AB Title compds. I [wherein R4-R6 and R8-R10 = H; R1, R2, and R3 = independently H, halo, carboxylic acid, trihalomethyl, or (un)substituted ester, amide, alkyl, alkoxy, or (hetero)aryl; R7 = (un)substituted alkyl or alkoxy; or pharmaceutically acceptable salt thereof] were prepared as modulators of the activity of protein kinases (PKs) and phosphatases. For example, 5-bromo-2-oxindole was coupled with 5-(3-diethylaminopropyl)-1H-indole-2-carbaldehyde (preparation given) in the presence of piperidine in EtOH to afford II, which inhibited GST-FLK-1, EGF receptor kinase, and PDGF with IC50 values of 0.03 μM, 2.87 μM, and 0.38 μM, resp. I are useful in treating disorders related to abnormal PK activity, such as blood vessel proliferative disorders, mesangial cell proliferative disorders, fibrotic disorders, cancer, diabetes, autoimmune disorders, hyperproliferation disorders, restenosis, fibrosis, psoriasis, von Heppel-Lindau disease, osteoarthritis, rheumatoid arthritis, angiogenesis, inflammatory disorders, immunol. disorders, and cardiovascular disorders (no data). Combinatorial libraries comprising at least five indolinone compds., formed by reacting oxindoles with aldehydes, are also claimed.

IT 258830-88-5P
RL: CPN (Combinatorial preparation); CRT (Combinatorial reactant); RCT (Reactant); SPN (Synthetic preparation); CMBI (Combinatorial study); PREP (Preparation); RACT (Reactant or reagent)
(preparation of (indolylmethylene)indolinones as protein kinase/phosphatase inhibitors for treatment of proliferative diseases)

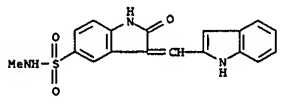
RN 258830-88-5 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-3-(1H-indol-2-ylmethylene)-N,N-dimethyl-2-oxo- (9CI) (CA INDEX NAME)

L4 ANSWER 22 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

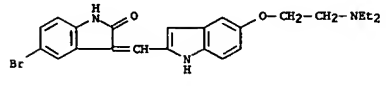


IT 258830-79-4P 380241-29-2P 380241-30-5P
380241-31-6P 380241-33-8P
RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
(preparation of (indolylmethylene)indolinones as protein kinase/phosphatase inhibitors for treatment of proliferative diseases)

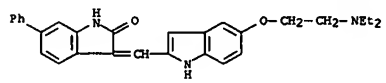
RN 258830-79-4 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-3-(1H-indol-2-ylmethylene)-N-methyl-2-oxo- (9CI) (CA INDEX NAME)



RN 380241-29-2 CAPLUS
CN 2H-Indol-2-one, 5-bromo-3-[[5-[2-(diethylamino)ethoxy]-1H-indol-2-yl]methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

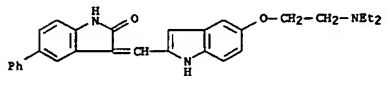


RN 380241-30-5 CAPLUS
CN 2H-Indol-2-one, 3-[[5-[2-(diethylamino)ethoxy]-1H-indol-2-yl]methylene]-1,3-dihydro-6-phenyl- (9CI) (CA INDEX NAME)

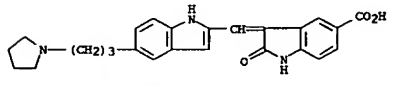


RN 380241-31-6 CAPLUS
CN 2H-Indol-2-one, 3-[[5-[2-(diethylamino)ethoxy]-1H-indol-2-yl]methylene]-1,3-dihydro-5-phenyl- (9CI) (CA INDEX NAME)

L4 ANSWER 22 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

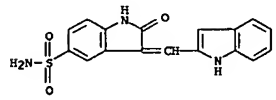


RN 380241-33-8 CAPLUS
CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-2-oxo-3-[[5-[3-(1-pyrrolidinyl)propyl]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

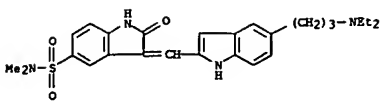


IT 258830-66-9P 380242-44-4P 380242-45-5P
380242-46-6P 380242-47-7P 380242-48-8P
380242-49-9P 380242-50-2P 380242-51-3P
380242-52-4P 380242-53-5P 380242-54-6P
380242-55-7P 380242-56-8P 380242-57-9P
380242-58-0P 380242-59-1P 380242-60-4P
380242-61-5P 380242-62-6P 380242-63-7P
380242-64-8P 380242-65-9P 380242-66-0P
380242-67-1P 380242-68-2P 380242-69-3P
380242-70-6P 380242-71-7P 380242-72-8P
380242-73-9P 380363-16-6P
RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
(preparation of (indolylmethylene)indolinones as protein kinase/phosphatase inhibitors for treatment of proliferative diseases)

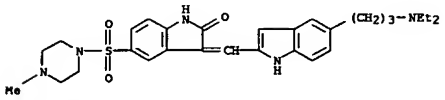
RN 258830-66-9 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-3-(1H-indol-2-ylmethylene)-2-oxo- (9CI) (CA INDEX NAME)



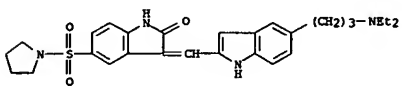
RN 380242-44-4 CAPLUS
CN 1H-Indole-5-sulfonamide, 3-[[5-[3-(diethylamino)propyl]-1H-indol-2-yl]methylene]-2,3-dihydro-N,N-dimethyl-2-oxo- (9CI) (CA INDEX NAME)



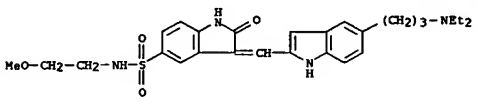
RN 380242-45-5 CAPLUS
CN Piperazine, 1-[[3-[[5-[3-(diethylamino)propyl]-1H-indol-2-yl]methylene]-2,3-dihydro-2-oxo-1H-indol-5-yl]sulfonyl]-4-methyl- (9CI) (CA INDEX NAME)



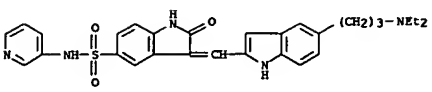
RN 380242-46-6 CAPLUS
CN Pyrrolidine, 1-[[3-[[5-[3-(diethylamino)propyl]-1H-indol-2-yl]methylene]-2,3-dihydro-2-oxo-1H-indol-5-yl]sulfonyl]- (9CI) (CA INDEX NAME)



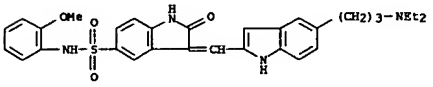
RN 380242-47-7 CAPLUS
CN 1H-Indole-5-sulfonamide, 3-[[5-[3-(diethylamino)propyl]-1H-indol-2-yl]methylene]-2,3-dihydro-N-(2-methoxyethyl)-2-oxo- (9CI) (CA INDEX NAME)



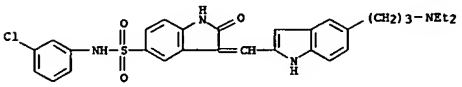
RN 380242-48-8 CAPLUS
CN 1H-Indole-5-sulfonamide, 3-[[5-[3-(diethylamino)propyl]-1H-indol-2-yl]methylene]-2,3-dihydro-2-oxo-N-3-pyridinyl- (9CI) (CA INDEX NAME)



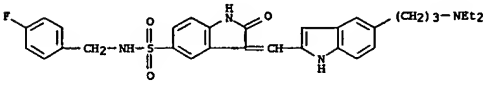
RN 380242-49-9 CAPLUS
CN 1H-Indole-5-sulfonamide, 3-[[5-[3-(diethylamino)propyl]-1H-indol-2-yl]methylene]-2,3-dihydro-N-(2-methoxyphenyl)-2-oxo- (9CI) (CA INDEX NAME)



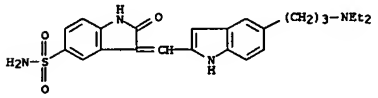
RN 380242-50-2 CAPLUS
CN 1H-Indole-5-sulfonamide, N-(3-chlorophenyl)-3-[[5-[3-(diethylamino)propyl]-1H-indol-2-yl]methylene]-2,3-dihydro-2-oxo- (9CI) (CA INDEX NAME)



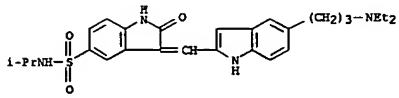
RN 380242-51-3 CAPLUS
CN 1H-Indole-5-sulfonamide, 3-[[5-[3-(diethylamino)propyl]-1H-indol-2-yl]methylene]-N-[(4-fluorophenyl)methyl]-2,3-dihydro-2-oxo- (9CI) (CA INDEX NAME)



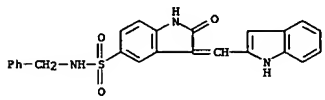
RN 380242-52-4 CAPLUS
CN 1H-Indole-5-sulfonamide, 3-[[5-[3-(diethylamino)propyl]-1H-indol-2-yl]methylene]-2,3-dihydro-2-oxo- (9CI) (CA INDEX NAME)



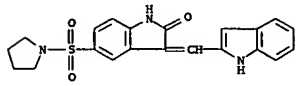
RN 380242-53-5 CAPLUS
CN 1H-Indole-5-sulfonamide, 3-[[5-[3-(diethylamino)propyl]-1H-indol-2-yl]methylene]-2,3-dihydro-N-(1-methylethyl)-2-oxo- (9CI) (CA INDEX NAME)



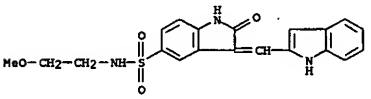
RN 380242-54-6 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-3-(1H-indol-2-ylmethylene)-2-oxo-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



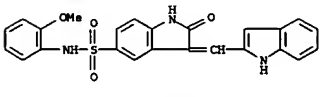
RN 380242-55-7 CAPLUS
CN Pyrrolidine, 1-[[2,3-dihydro-3-(1H-indol-2-ylmethylene)-2-oxo-1H-indol-5-yl]sulfonyl]- (9CI) (CA INDEX NAME)



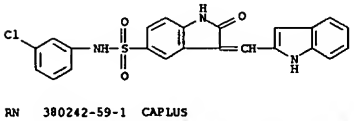
RN 380242-56-8 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-3-(1H-indol-2-ylmethylene)-N-(2-methoxyethyl)-2-oxo- (9CI) (CA INDEX NAME)



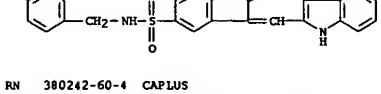
RN 380242-57-9 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-3-(1H-indol-2-ylmethylene)-N-(2-methoxyphenyl)-2-oxo- (9CI) (CA INDEX NAME)



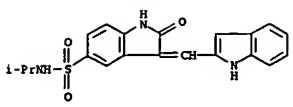
RN 380242-58-0 CAPLUS
CN 1H-Indole-5-sulfonamide, N-(3-chlorophenyl)-2,3-dihydro-3-(1H-indol-2-ylmethylene)-2-oxo- (9CI) (CA INDEX NAME)



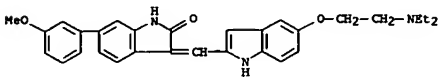
RN 380242-59-1 CAPLUS
CN 1H-Indole-5-sulfonamide, N-[(4-fluorophenyl)methyl]-2,3-dihydro-3-(1H-indol-2-ylmethylene)-2-oxo- (9CI) (CA INDEX NAME)



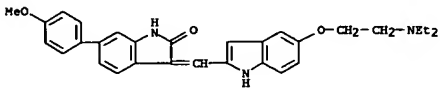
RN 380242-60-4 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-3-(1H-indol-2-ylmethylene)-N-(1-methylethyl)-2-oxo- (9CI) (CA INDEX NAME)



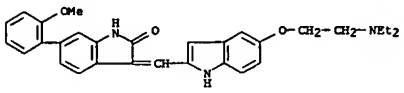
RN 380242-61-5 CAPLUS
CN 2H-Indol-2-one, 3-[[5-[2-(diethylamino)ethoxy]-1H-indol-2-yl]methylene]-1,3-dihydro-6-(3-methoxyphenyl)- (9CI) (CA INDEX NAME)



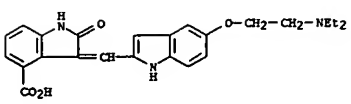
RN 380242-62-6 CAPLUS
CN 2H-Indol-2-one, 3-[[5-[2-(diethylamino)ethoxy]-1H-indol-2-yl]methylene]-1,3-dihydro-6-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



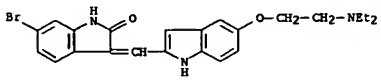
RN 380242-63-7 CAPLUS
CN 2H-Indol-2-one, 3-[[5-[2-(diethylamino)ethoxy]-1H-indol-2-yl]methylene]-1,3-dihydro-6-(2-methoxyphenyl)- (9CI) (CA INDEX NAME)



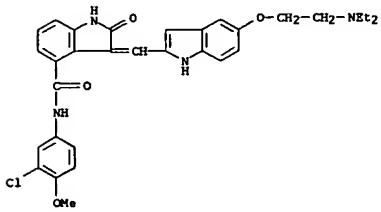
RN 380242-64-8 CAPLUS
CN 1H-Indole-4-carboxylic acid, 3-[[5-[2-(diethylamino)ethoxy]-1H-indol-2-yl]methylene]-2,3-dihydro-2-oxo- (9CI) (CA INDEX NAME)



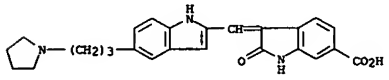
RN 380242-65-9 CAPLUS
CN 2H-Indol-2-one, 6-bromo-3-[[5-[2-(diethylamino)ethoxy]-1H-indol-2-yl]methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)



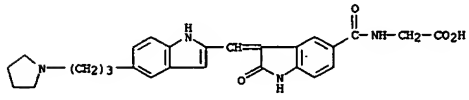
RN 380242-66-0 CAPLUS
CN 1H-Indole-4-carboxamide, N-(3-chloro-4-methoxyphenyl)-3-[[5-[2-(diethylamino)ethoxy]-1H-indol-2-yl]methylene]-2,3-dihydro-2-oxo- (9CI) (CA INDEX NAME)



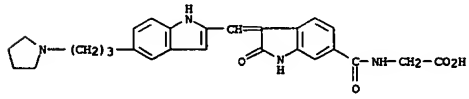
RN 380242-67-1 CAPLUS
CN 1H-Indole-6-carboxylic acid, 2,3-dihydro-2-oxo-3-[[5-[3-(1-pyrrolidinyl)propyl]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)



RN 380242-68-2 CAPLUS
CN Glycine, N-[[2,3-dihydro-2-oxo-3-[[5-[3-(1-pyrrolidinyl)propyl]-1H-indol-2-yl]methylene]-1H-indol-5-yl]carbonyl]- (9CI) (CA INDEX NAME)

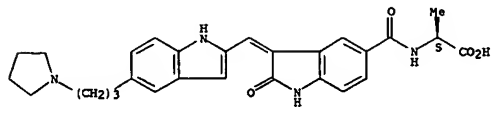


RN 380242-69-3 CAPLUS
CN Glycine, N-[[2,3-dihydro-2-oxo-3-[[5-[3-(1-pyrrolidinyl)propyl]-1H-indol-2-yl]methylene]-1H-indol-6-yl]carbonyl]- (9CI) (CA INDEX NAME)



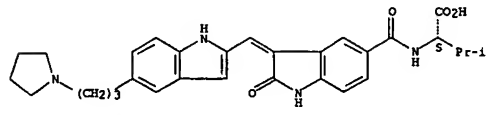
RN 380242-70-6 CAPLUS
CN L-Alanine, N-[[2,3-dihydro-2-oxo-3-[[5-[3-(1-pyrrolidinyl)propyl]-1H-indol-2-yl]methylene]-1H-indol-5-yl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 380242-71-7 CAPLUS
CN L-Valine, N-[[2,3-dihydro-2-oxo-3-[[5-[3-(1-pyrrolidinyl)propyl]-1H-indol-2-yl]methylene]-1H-indol-5-yl]carbonyl]- (9CI) (CA INDEX NAME)

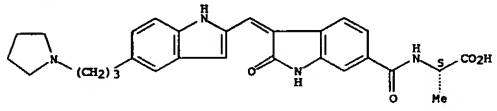
Absolute stereochemistry.
Double bond geometry unknown.



RN 380242-72-8 CAPLUS

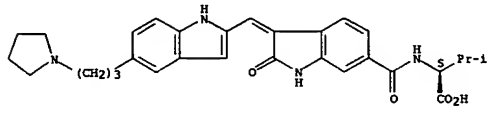
CN L-Alanine, N-[[2,3-dihydro-2-oxo-3-[[5-[3-(1-pyrrolidinyl)propyl]-1H-indol-2-yl]methylene]-1H-indol-6-yl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

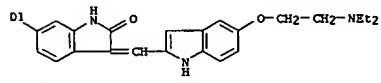


RN 380242-73-9 CAPLUS
CN L-Valine, N-[[2,3-dihydro-2-oxo-3-[[5-[3-(1-pyrrolidinyl)propyl]-1H-indol-2-yl]methylene]-1H-indol-6-yl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



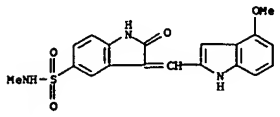
RN 380363-16-6 CAPLUS
CN 2H-Indol-2-one, 3-[[5-[2-(diethylamino)ethoxy]-1H-indol-2-yl]methylene]-1,3-dihydro-6-(pyridinyl)- (9CI) (CA INDEX NAME)



IT 380242-01-3P
RL: CRT (Combinatorial reactant); RCT (Reactant); SPN (Synthetic preparation); CMBI (Combinatorial study); PREP (Preparation); RACT (Reactant or reagent)
(preparation of (indolylmethylene)indolinones as protein kinase/phosphatase inhibitors for treatment of proliferative diseases)

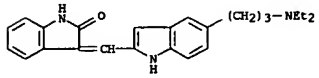
RN 380242-01-3 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-3-[(4-methoxy-1H-indol-2-

yl)methylene]-N-methyl-2-oxo- (9CI) (CA INDEX NAME)

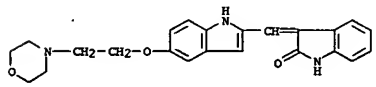


IT 380241-13-4P 380241-14-5P 380241-15-6P
380241-16-7P 380241-17-8P 380241-18-9P
380241-19-0P 380241-20-3P 380241-21-4P
380241-22-5P 380241-23-6P 380241-24-7P
380241-25-8P 380241-26-9P 380241-27-0P
380241-28-1P 380241-32-7P 380241-34-9P
380241-35-0P 380241-36-1P 380241-37-2P
380241-38-3P 380241-39-4P 380241-40-7P
380241-41-8P 380241-42-9P 380241-43-0P
380241-44-1P 380241-45-2P 380241-46-3P
380241-47-4P 380241-48-5P 380241-49-6P
380241-50-9P 380241-51-0P 380241-53-2P
380241-54-3P 380241-56-5P 380241-59-8P
380241-61-2P 380241-65-6P 380241-68-9P
380241-71-4P 380241-74-7P 380241-78-1P
380241-82-7P 380241-84-9P 380241-86-1P
380241-88-3P 380241-90-7P 380241-91-8P
380241-92-9P 380241-93-0P 380241-94-1P
380241-95-2P 380241-96-3P 380241-97-4P
380241-98-5P 380241-99-6P 380242-00-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (indolylmethylene)indolinones as protein kinase/phosphatase
inhibitors for treatment of proliferative diseases)

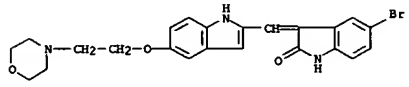
RN 380241-13-4 CAPLUS
CN 2H-Indol-2-one, 3-[[5-[3-(diethylamino)propyl]-1H-indol-2-yl]methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)



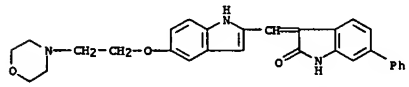
RN 380241-14-5 CAPLUS
CN 2H-Indol-2-one, 5-bromo-3-[[5-[3-(diethylamino)propyl]-1H-indol-2-yl]methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)



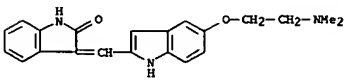
RN 380241-20-3 CAPLUS
CN 2H-Indol-2-one, 5-bromo-1,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)



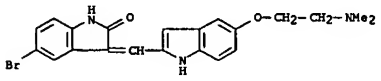
RN 380241-21-4 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-6-phenyl- (9CI) (CA INDEX NAME)



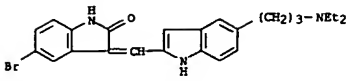
RN 380241-22-5 CAPLUS
CN 2H-Indol-2-one, 3-[[5-[2-(dimethylamino)ethoxy]-1H-indol-2-yl]methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)



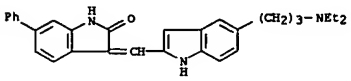
RN 380241-23-6 CAPLUS
CN 2H-Indol-2-one, 5-bromo-3-[[5-[2-(dimethylamino)ethoxy]-1H-indol-2-yl]methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)



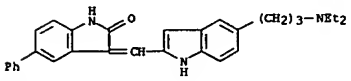
RN 380241-24-7 CAPLUS



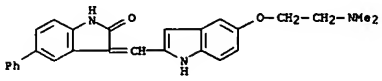
RN 380241-15-6 CAPLUS
CN 2H-Indol-2-one, 3-[[5-[3-(diethylamino)propyl]-1H-indol-2-yl]methylene]-1,3-dihydro-6-phenyl- (9CI) (CA INDEX NAME)



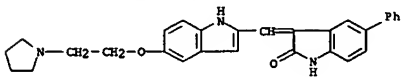
RN 380241-16-7 CAPLUS
CN 2H-Indol-2-one, 3-[[5-[3-(diethylamino)propyl]-1H-indol-2-yl]methylene]-1,3-dihydro-5-phenyl- (9CI) (CA INDEX NAME)



RN 380241-17-8 CAPLUS
CN 2H-Indol-2-one, 3-[[5-[2-(dimethylamino)ethoxy]-1H-indol-2-yl]methylene]-1,3-dihydro-5-phenyl- (9CI) (CA INDEX NAME)

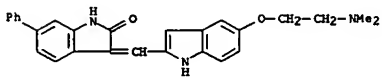


RN 380241-18-9 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-5-phenyl-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

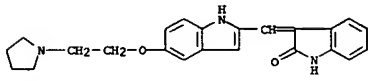


RN 380241-19-0 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

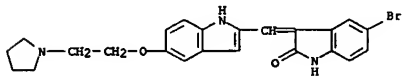
CN 2H-Indol-2-one, 3-[[5-[2-(dimethylamino)ethoxy]-1H-indol-2-yl]methylene]-1,3-dihydro-6-phenyl- (9CI) (CA INDEX NAME)



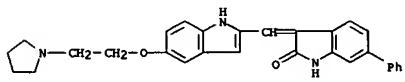
RN 380241-25-8 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)



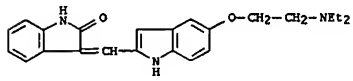
RN 380241-26-9 CAPLUS
CN 2H-Indol-2-one, 5-bromo-1,3-dihydro-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)



RN 380241-27-0 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-6-phenyl-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

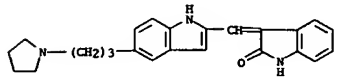


RN 380241-28-1 CAPLUS
CN 2H-Indol-2-one, 3-[[5-[2-(diethylamino)ethoxy]-1H-indol-2-yl]methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)



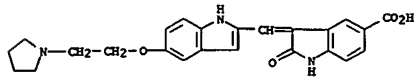
RN 380241-32-7 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[[5-[3-(1-pyrrolidinyl)propyl]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)



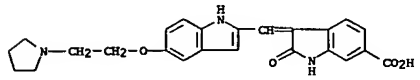
RN 380241-34-9 CAPLUS

CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-2-oxo-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)



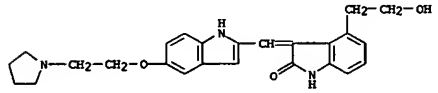
RN 380241-35-0 CAPLUS

CN 1H-Indole-6-carboxylic acid, 2,3-dihydro-2-oxo-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)



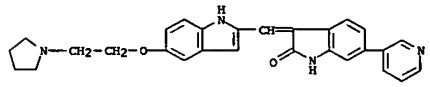
RN 380241-36-1 CAPLUS

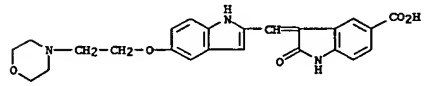
CN 2H-Indol-2-one, 1,3-dihydro-4-(2-hydroxyethyl)-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)



RN 380241-37-2 CAPLUS

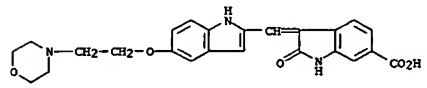
CN 2H-Indol-2-one, 1,3-dihydro-6-(3-pyridinyl)-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)





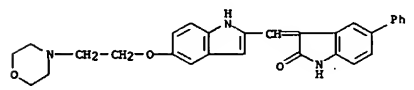
RN 380241-43-0 CAPLUS

CN 1H-Indole-6-carboxylic acid, 2,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-2-oxo- (9CI) (CA INDEX NAME)



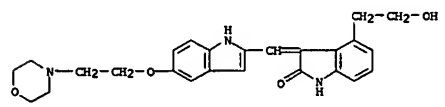
RN 380241-44-1 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-5-phenyl- (9CI) (CA INDEX NAME)



RN 380241-45-2 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-4-(2-hydroxyethyl)-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

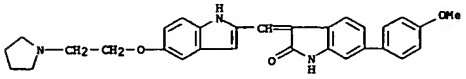


RN 380241-46-3 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-6-(3-pyridinyl)- (9CI) (CA INDEX NAME)

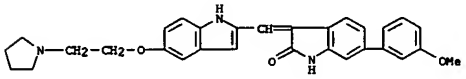
RN 380241-38-3 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-6-(4-methoxyphenyl)-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)



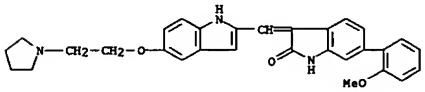
RN 380241-39-4 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-6-(3-methoxyphenyl)-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)



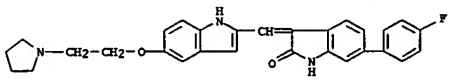
RN 380241-40-7 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-6-(2-methoxyphenyl)-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)



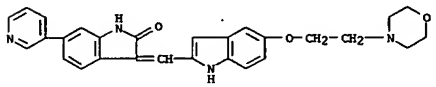
RN 380241-41-8 CAPLUS

CN 2H-Indol-2-one, 6-(4-fluorophenyl)-1,3-dihydro-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)



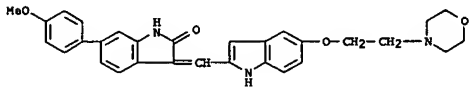
RN 380241-42-9 CAPLUS

CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-2-oxo- (9CI) (CA INDEX NAME)



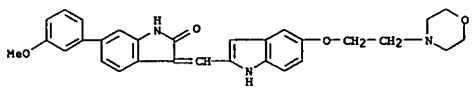
RN 380241-47-4 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-6-(4-methoxyphenyl)-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)



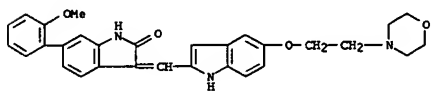
RN 380241-48-5 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-6-(3-methoxyphenyl)-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)



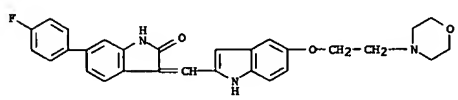
RN 380241-49-6 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-6-(2-methoxyphenyl)-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

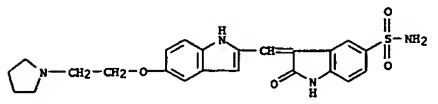


RN 380241-50-9 CAPLUS

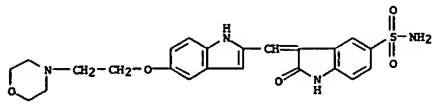
CN 2H-Indol-2-one, 6-(4-fluorophenyl)-1,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)



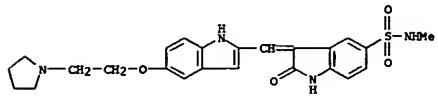
RN 380241-51-0 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-2-oxo-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)



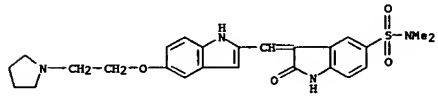
RN 380241-53-2 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-2-oxo- (9CI) (CA INDEX NAME)



RN 380241-54-3 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N-methyl-2-oxo-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)



RN 380241-56-5 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N,N-dimethyl-2-oxo-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)



RN 380241-59-8 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N-(1-methylethyl)-2-oxo-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

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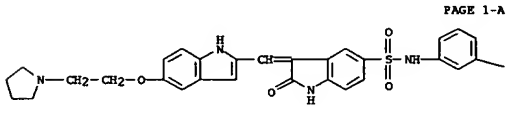

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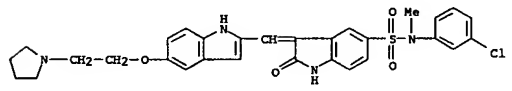
Cl

RN 380241-74-7 CAPLUS
CN 1H-Indole-5-sulfonamide, N-(3-chlorophenyl)-2,3-dihydro-N-methyl-2-oxo-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)



RN 380241-78-1 CAPLUS
CN 1H-Indole-5-sulfonamide, N-(4-chloro-2-fluorophenyl)-2,3-dihydro-2-oxo-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

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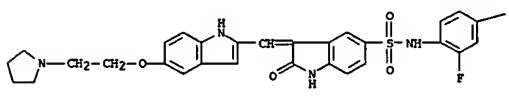

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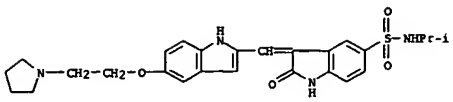
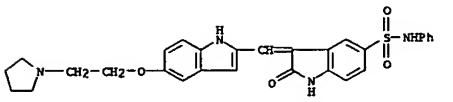
Cl

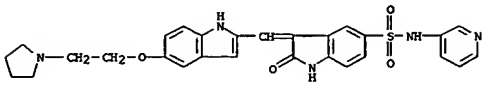
RN 380241-82-7 CAPLUS
CN Quinoline, 1-[[2,3-dihydro-2-oxo-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]-1H-indol-5-yl]sulfonyl]-1,2,3,4-tetrahydro- (9CI) (CA INDEX NAME)



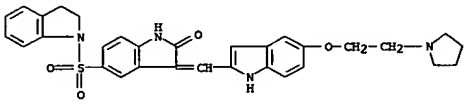
RN 380241-61-2 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-2-oxo-N-phenyl-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)



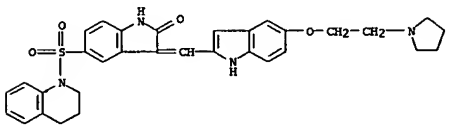
RN 380241-65-6 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-2-oxo-N-3-pyridinyl-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)



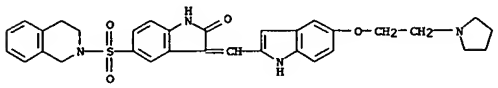
RN 380241-68-9 CAPLUS
CN 1H-Indole, 1-[[2,3-dihydro-2-oxo-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]-1H-indol-5-yl]sulfonyl]-2,3-dihydro- (9CI) (CA INDEX NAME)



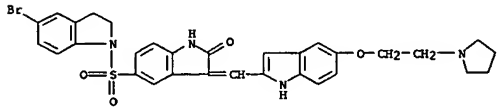
RN 380241-71-4 CAPLUS
CN 1H-Indole-5-sulfonamide, N-(3-chlorophenyl)-2,3-dihydro-2-oxo-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)



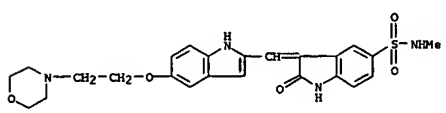
RN 380241-84-9 CAPLUS
CN Isoquinoline, 2-[[2,3-dihydro-2-oxo-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]-1H-indol-5-yl]sulfonyl]-1,2,3,4-tetrahydro- (9CI) (CA INDEX NAME)



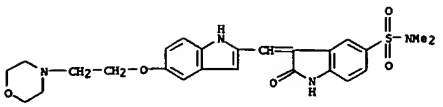
RN 380241-86-1 CAPLUS
CN 1H-Indole, 5-bromo-1-[[2,3-dihydro-2-oxo-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]-1H-indol-5-yl]sulfonyl]-2,3-dihydro- (9CI) (CA INDEX NAME)



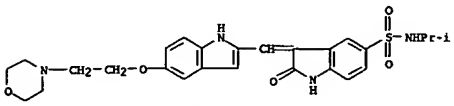
RN 380241-88-3 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N-methyl-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-2-oxo- (9CI) (CA INDEX NAME)



RN 380241-90-7 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N,N-dimethyl-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-2-oxo- (9CI) (CA INDEX NAME)



RN 380241-91-8 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N-(1-methylethyl)-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-2-oxo- (9CI) (CA INDEX NAME)



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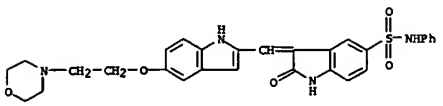
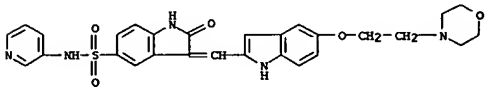
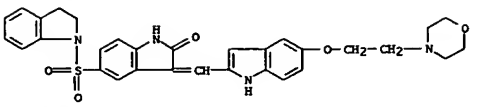
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-2-oxo-N-phenyl- (9CI) (CA INDEX NAME)



RN 380241-93-0 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-2-oxo-N-3-pyridinyl- (9CI) (CA INDEX NAME)



RN 380241-94-1 CAPLUS
CN 1H-Indole, 1-[[2,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-2-oxo-1H-indol-5-yl]sulfonyl]-2,3-dihydro- (9CI) (CA INDEX NAME)



RN 380241-95-2 CAPLUS
CN 1H-Indole-5-sulfonamide, N-(3-chlorophenyl)-2,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-2-oxo- (9CI) (CA INDEX NAME)

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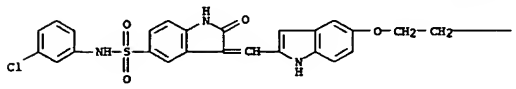

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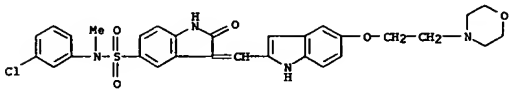
RN 380241-96-3 CAPLUS
CN 1H-Indole-5-sulfonamide, N-(3-chlorophenyl)-2,3-dihydro-N-methyl-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-2-oxo- (9CI) (CA INDEX NAME)



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CN 1H-Indole-5-sulfonamide, N-(4-chloro-2-fluorophenyl)-2,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-2-oxo- (9CI) (CA INDEX NAME)

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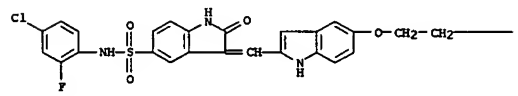

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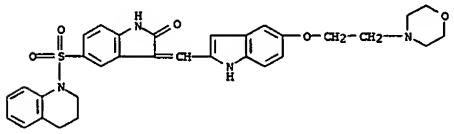
RN 380241-98-5 CAPLUS
CN Quinoline, 1-[[2,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-2-oxo-1H-indol-5-yl]sulfonyl]-1,2,3,4-tetrahydro- (9CI) (CA INDEX NAME)



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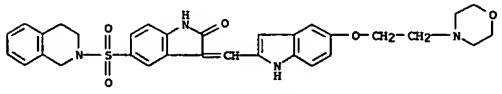
CN Isoquinoline, 2-[[2,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-2-oxo-1H-indol-5-yl]sulfonyl]-1,2,3,4-tetrahydro- (9CI) (CA INDEX NAME)



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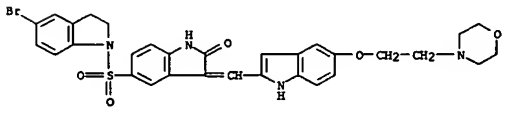

L4 ANSWER 23 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:472477 CAPLUS
DOCUMENT NUMBER: 135:56059
TITLE: Methods of modulating c-kit tyrosine protein kinase function with indolinone compounds
INVENTOR(S): Lipson, Ken; McMahon, Gerald
PATENT ASSIGNEE(S): Sugen, Inc., USA
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
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PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001045689	A2	20010628	WO 2000-US35009	20001222
WO 2001045689	A3	20020103		
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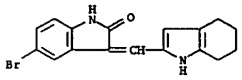
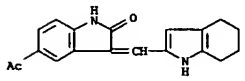
US 2002010203	A1	20020124	US 2000-741842	20001222
EP 1255536	A2	20021113	EP 2000-991704	20001222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004500363	T2	20040108	JP 2001-546428	20001222
NZ 519697	A	20040827	NZ 2000-519697	20001222
US 2004002534	A1	20040101	US 2003-600868	20030623
PRIORITY APPLN. INFO.:			US 1999-171693P	P 19991222
			US 2000-741842	B1 20001222
			WO 2000-US35009	W 20001222

OTHER SOURCE(S): MARPAT 135:56059
AB The invention concerns indolinone compds. and their use to inhibit the activity of a receptor tyrosine kinase. The invention is preferably used to treat cell proliferative disorders such as cancers characterized by over-activity or inappropriate activity of c-kit kinase.
IT 204003-89-4 290821-18-0 330161-87-0
330161-88-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(indolinone derivs. for c-kit tyrosine protein kinase function modulation)
RN 204003-89-4 CAPLUS
CN 2H-Indol-2-one, 5-bromo-1,3-dihydro-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)

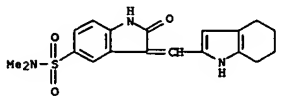


L4 ANSWER 23 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

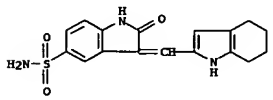
RN 290821-18-0 CAPLUS
CN 2H-Indol-2-one, 5-acetyl-1,3-dihydro-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



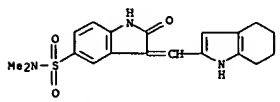
RN 330161-87-0 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N,N-dimethyl-2-oxo-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



RN 330161-88-1 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-2-oxo-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)

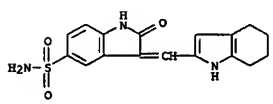


L4 ANSWER 24 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:215821 CAPLUS
DOCUMENT NUMBER: 134:232275
TITLE: SU6656, a selective Src family kinase inhibitor, used to probe growth factor signaling
AUTHOR(S): Blake, Robert A.; Broome, Martin A.; Liu, Xiangdong; Wu, Jianming; Gishizky, Mikhail; Sun, Li; Courtneidge, Sara A.
CORPORATE SOURCE: Sugen Inc., South San Francisco, CA, 94080, USA
SOURCE: Molecular and Cellular Biology (2000), 20(23), 9018-9027
CODEN: MCEBD4; ISSN: 0270-7306
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The use of small-mol. inhibitors to study mol. components of cellular signal transduction pathways provides a means of anal. complementary to currently used techniques, such as antisense, dominant-neg. (interfering) mutants and constitutively activated mutants. The authors have identified and characterized a small-mol. inhibitor, SU6656, which exhibits selectivity for Src and other members of the Src family. A related inhibitor, SU6657, inhibits many kinases, including Src and the platelet-derived growth factor (PDGF) receptor. The use of SU6656 confirmed the authors' previous findings that Src family kinases are required for both Myc induction and DNA synthesis in response to PDGF stimulation of NIH 3T3 fibroblasts. By comparing PDGF-stimulated tyrosine phosphorylation events in untreated and SU6656-treated cells, the authors found that some substrates (for example, c-Cbl, and protein kinase C8) were Src family substrates, whereas others (for example, phospholipase C-γ) were not. One protein, the adaptor Shc, was a substrate for both Src family kinases (on tyrosines 239 and 240) and a distinct tyrosine kinase (on tyrosine 317, which is perhaps phosphorylated by the PDGF receptor itself). Microinjection expts. demonstrated that a Shc mol. carrying mutations of tyrosines 239 and 240, in conjunction with an SH2 domain mutation, interfered with PDGF-stimulated DNA synthesis. Deletion of the phosphotyrosine-binding domain also inhibited synthesis. These inhibitions were overcome by heterologous expression of Myc, supporting the hypothesis that Shc functions in the Src pathway. SU6656 should prove a useful addnl. tool for further dissecting the role of Src kinases in this and other signal transduction pathways.
IT 330161-87-0, SU 6656 330161-88-1, SU 6657
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); FRP (Properties); BIOL (Biological study)
(identification and characterization of small-mol. inhibitor SU6656 in relation to selective Src family kinase inhibitor SU6656 used to probe growth factor signaling)
RN 330161-87-0 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N,N-dimethyl-2-oxo-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



RN 330161-88-1 CAPLUS

L4 ANSWER 24 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-2-oxo-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 25 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:622463 CAPLUS
DOCUMENT NUMBER: 133:217719
TITLE: 3-(Cyclohexanoheteroarylidenyl)-2-indolinone protein tyrosine kinase inhibitors, and their therapeutic use
INVENTOR(S): Tang, Peng Cho; Sun, Li; McMahon, Gerald; Blake, Robert A.
PATENT ASSIGNEE(S): Sugen, Inc., USA
SOURCE: U.S., 61 pp., Cont. -in-part of U.S. Ser. No. 99,842.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6114371	A	20000905	US 1998-190970	19981112
US 6130238	A	20001010	US 1998-99842	19980619
US 2002183370	A1	20021205	US 2001-29946	20011231
US 6579897	B2	20030617		

PRIORITY APPLN. INFO.:

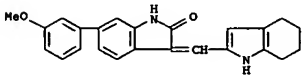
US 1997-50977P	P	19970620
US 1997-59384P	P	19970919
US 1998-99842	A2	19980619
US 1997-50413P	P	19970620
US 1997-59544P	P	19970919
US 1998-99721	A1	19980619
US 2000-482198	A3	20000112

OTHER SOURCE(S): CASREACT 133:217719; MARPAT 133:217719

AB 3-(Cyclohexano-heteroarylidenyl)-2-indolinone compds., and physiol. acceptable salts and prodrugs thereof, are disclosed which are expected to modulate the activity of protein tyrosine kinases and therefore to be useful in the prevention and treatment of protein tyrosine kinase-related cellular disorders (cancer, arthritis, restenosis, etc.).

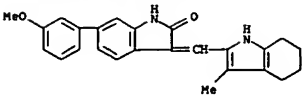
IT **245035-88-5 245035-93-2 245035-96-5**
245036-00-4 245036-07-1 245036-08-2
245036-21-9 245036-22-0 290821-14-6
290821-15-7 290821-16-8 290821-17-9
290821-18-0 290821-19-1 290821-20-4
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclohexanoheteroarylidenyl indolinone protein tyrosine kinase inhibitors, and therapeutic use)

RN 245035-88-5 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-6-(3-methoxyphenyl)-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)

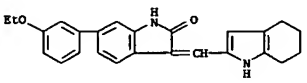


RN 245035-93-2 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-6-(3-methoxyphenyl)-3-[(4,5,6,7-tetrahydro-3-methyl-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)

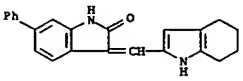
L4 ANSWER 25 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



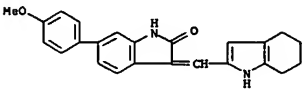
RN 245035-96-5 CAPLUS
CN 2H-Indol-2-one, 6-(3-ethoxyphenyl)-1,3-dihydro-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



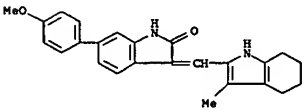
RN 245036-00-4 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-6-phenyl-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



RN 245036-07-1 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-6-(4-methoxyphenyl)-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)

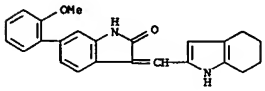


RN 245036-08-2 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-6-(4-methoxyphenyl)-3-[(4,5,6,7-tetrahydro-3-methyl-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)

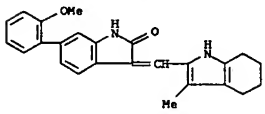


L4 ANSWER 25 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

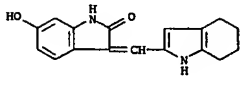
RN 245036-21-9 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-6-(2-methoxyphenyl)-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



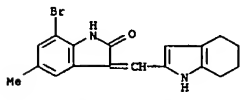
RN 245036-22-0 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-6-(2-methoxyphenyl)-3-[(4,5,6,7-tetrahydro-3-methyl-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



RN 290821-14-6 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-6-hydroxy-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)

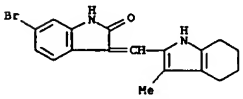


RN 290821-15-7 CAPLUS
CN 2H-Indol-2-one, 7-bromo-1,3-dihydro-5-methyl-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)

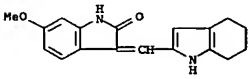


RN 290821-16-8 CAPLUS
CN 2H-Indol-2-one, 6-bromo-1,3-dihydro-3-[(4,5,6,7-tetrahydro-3-methyl-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)

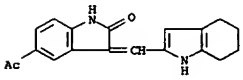
L4 ANSWER 25 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



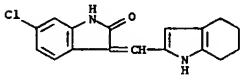
RN 290821-17-9 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-6-methoxy-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



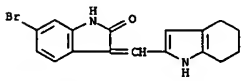
RN 290821-18-0 CAPLUS
CN 2H-Indol-2-one, 5-acetyl-1,3-dihydro-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



RN 290821-19-1 CAPLUS
CN 2H-Indol-2-one, 6-chloro-1,3-dihydro-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



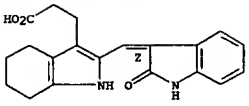
RN 290821-20-4 CAPLUS
CN 2H-Indol-2-one, 6-bromo-1,3-dihydro-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

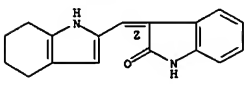
ACCESSION NUMBER: 2000:417312 CAPLUS
DOCUMENT NUMBER: 133:159618
TITLE: Identification of Substituted 3-[(4,5,6,7-Tetrahydro-1H-indol-2-yl)methylene]-1,3-dihydroindol-2-ones as Growth Factor Receptor Inhibitors for VEGF-R2 (Flk-1/KDR), FGF-R1, and PDGF-Rβ Tyrosine Kinases
AUTHOR(S): Sun, Li; Tran, Ngoc; Liang, Congxing; Hubbard, Steve; Tang, Flora; Lipson, Kenneth; Schreck, Randall; Zhou, Yong; McMahon, Gerald; Tang, Cho
CORPORATE SOURCE: SUGEN Inc., South San Francisco, CA, 94080-4811, USA
SOURCE: Journal of Medicinal Chemistry (2000), 43(14), 2655-2663
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A series of new 3-substituted indolin-2-ones containing a tetrahydroindole moiety was developed as specific inhibitors of receptor tyrosine kinases associated with VEGF-R, FGF-R, and PDGF-R growth factor receptors. These compds. were evaluated for their inhibitory properties toward VEGF-R2 (Flk-1/KDR), FGF-R1, PDGF-Rβ, p60c-Src, and EGF-R tyrosine kinases and their ability to inhibit growth factor-dependent cell proliferation. Structure-activity relationships of this new pharmacophore have been determined at the level of kinase inhibition. Compds. containing a propionic acid moiety at the C-3' position of the tetrahydroindole ring represented the most potent indolin-2-ones to inactivate the VEGF, FGF, and PDGF receptor kinases. The inhibitory activities of 3-[3-(2-carboxyethyl)-4,5,6,7-tetrahydro-1H-indol-2-ylmethylene]-2-oxo-2,3-dihydro-1H-indole-5-carboxylic acid against VEGF-R2 (Flk-1), 3-{2-[6-(2-methoxyphenyl)-2-oxo-1,2-dihydroindol-3-ylidenemethyl]-4,5,6,7-tetrahydro-1H-indol-3-yl}propionic acid against FGF-R1, and 3-[2-(5-bromo-2-oxo-1,2-dihydroindol-3-ylidenemethyl)-4,5,6,7-tetrahydro-1H-indol-3-yl]propionic acid (I) against PDGF-Rβ were 4, 80, and 4 nM, resp. However, all of these compds. were inactive when tested against the EGF-R tyrosine kinase. Compds. 3-[2-(2-oxo-1,2-dihydroindol-3-ylidenemethyl)-4,5,6,7-tetrahydro-1H-indol-3-yl]propionic acid (II) and I represented the most potent inhibitors of these classes to inhibit both biochem. kinase and growth factor-dependent cell proliferation for these three targets. In addition, compound II was cocrystd. with the catalytic domain of FGF-R1 providing evidence to explain the structure-activity relation results. This study has provided evidence to support the potential of these new tyrosine kinase inhibitors for the treatment of angiogenesis and other growth factor-related diseases including human cancers.
IT **288144-28-5P**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(substituted [(tetrahydroindolyl)methylene]dihydroindolones as growth factor receptor inhibitors for VEGF-R2 (Flk-1/KDR) and FGF-R1, and PDGF-Rβ tyrosine kinases and as inhibitors of growth factor-dependent cell proliferation)
RN 288144-28-5 CAPLUS
CN 1H-Indole-3-propanoic acid, 2-[(Z)-(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



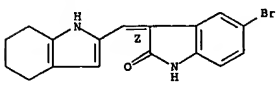
IT **288144-19-4P 288144-20-7P 288144-21-8P**
288144-22-9P 288144-23-0P 288144-24-1P
288144-25-2P 288144-26-3P 288144-27-4P
288144-29-6P 288144-30-9P 288144-31-0P
288144-32-1P 288144-33-2P 288144-34-3P
288144-35-4P 288144-36-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(substituted [(tetrahydroindolyl)methylene]dihydroindolones as growth factor receptor inhibitors for VEGF-R2 (Flk-1/KDR) and FGF-R1, and PDGF-Rβ tyrosine kinases and as inhibitors of growth factor-dependent cell proliferation)
RN 288144-19-4 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



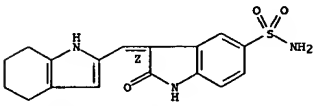
RN 288144-20-7 CAPLUS
CN 2H-Indol-2-one, 5-bromo-1,3-dihydro-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



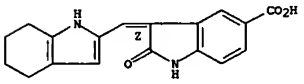
RN 288144-21-8 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-2-oxo-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



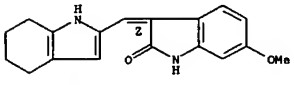
RN 288144-22-9 CAPLUS
CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-2-oxo-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



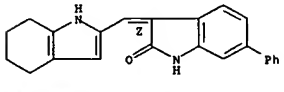
RN 288144-23-0 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-6-methoxy-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



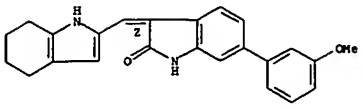
RN 288144-24-1 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-6-phenyl-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



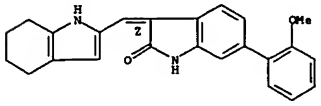
RN 288144-25-2 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-6-(3-methoxyphenyl)-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



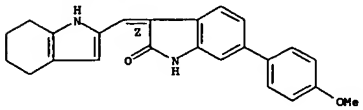
RN 288144-26-3 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-6-(2-methoxyphenyl)-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



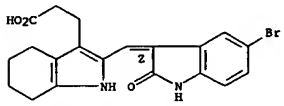
RN 288144-27-4 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-6-(4-methoxyphenyl)-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



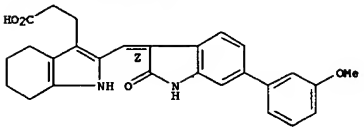
RN 288144-29-6 CAPLUS
CN 1H-Indole-3-propanoic acid, 2-[(Z)-(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



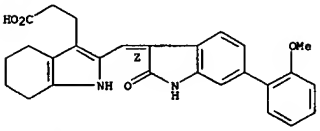
RN 288144-30-9 CAPLUS
CN 1H-Indole-3-propanoic acid, 2-[(Z)-[5-(aminosulfonyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



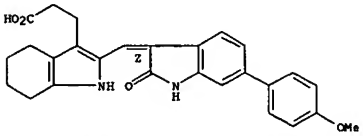
RN 288144-35-4 CAPLUS
CN 1H-Indole-3-propanoic acid, 2-[(Z)-[1,2-dihydro-6-(2-methoxyphenyl)-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



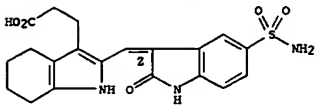
RN 288144-36-5 CAPLUS
CN 1H-Indole-3-propanoic acid, 2-[(Z)-[1,2-dihydro-6-(4-methoxyphenyl)-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



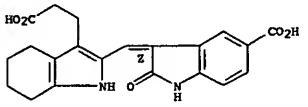
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Double bond geometry as shown.



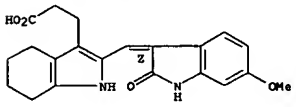
RN 288144-31-0 CAPLUS
CN 1H-Indole-3-propanoic acid, 2-[(Z)-(5-carboxy-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



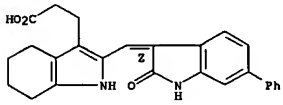
RN 288144-32-1 CAPLUS
CN 1H-Indole-3-propanoic acid, 2-[(Z)-(1,2-dihydro-6-methoxy-2-oxo-3H-indol-3-ylidene)methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 288144-33-2 CAPLUS
CN 1H-Indole-3-propanoic acid, 2-[(Z)-(1,2-dihydro-2-oxo-6-phenyl-3H-indol-3-ylidene)methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 288144-34-3 CAPLUS
CN 1H-Indole-3-propanoic acid, 2-[(Z)-[1,2-dihydro-6-(3-methoxyphenyl)-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)

ACCESSION NUMBER: 2000:117197 CAPLUS
DOCUMENT NUMBER: 132:166123
TITLE: 3-Methylidenyl-2-indolinone modulators of protein kinase
INVENTOR(S): Tang, Peng Cho; Sun, Li; Miller, Todd Anthony; Liang, Congxin; Tran, Ngoc My; Nguyen, Anh Thi; Nematalla, Asaad
PATENT ASSIGNEE(S): Sugen, Inc., USA
SOURCE: PCT Int. Appl., 347 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000008202	A2	20000217	WO 1999-US17845	19990804
WO 2000008202	A3	20000518		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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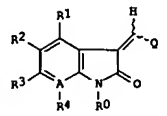
AU 9954684	A1	20000228	AU 1999-54684	19990804
JP 2002522452	T2	20020723	JP 2000-563824	19990804
US 6531502	B1	20030311	US 2001-762198	20010205
US 2002183364	A1	20021205	US 2001-13944	20011213
US 6680335	B2	20040120		
US 2004024010	A1	20040205	US 2003-383690	20030310
US 6855730	B2	20050215		
US 2004067531	A1	20040408	US 2003-458730	20030611
PRIORITY APPLN. INFO.:			US 1998-129256 A	19980804
			US 1998-95470P P	19980805
			US 1998-102178P P	19980928
			US 1999-116107P P	19990115
			US 1997-915366 A2	19970820
			US 1998-72023P P	19980121
			WO 1999-US17845 W	19990804
			US 1999-407164 A1	19990928
			US 2001-762198 A3	20010205

OTHER SOURCE(S): MARPAT 132:166123
GI



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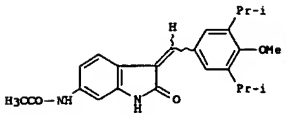


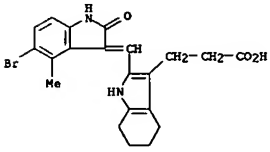
II

AB The title compds. (I) [wherein A = C or N; Q = substituted Ph, pyrrolyl, or indolyl; R0 = H, alkyl, C(O)R19, or C(O)OR19; R1 = H, (un)substituted alkyl, alkoxy, halo, aryl, (CH2)nOC(O)R19, or C(O)NR19; R2 = H, (cyclo)alkyl, (hetero)aryl, heteroalicyclic, trihalomethyl, alkoxy, halo, sulfamido, C(O)OR19, C(O)R19, NHC(O)OR19, (un)substituted amino, etc.; R3 = H, alkyl, trihalomethyl, alkoxy, aryl(oxy), heteroaryl, heteroalicyclic, OH, halo, sulfamido, C(O)R19, (un)substituted amino, etc.; R4 = H, alkyl, alkoxy, or halo; R19 = H, (cyclo)alkyl, alkenyl, alkynyl, or aryl; n = 1-4] were prepared as modulators of the activity of receptor tyrosine kinases (RTKs), non-receptor protein tyrosine kinases (CTKs), and serine/threonine protein kinases (STKs). Examples include over 200 syntheses and data from seventeen bioassays. For instance, II was prepared by a 3-step sequence involving: (1) cyclization and reduction of 2,4-dinitrophenylacetic acid with SnCl2.2H2O in EtOH to form 6-amino-2-oxindole, (2) amidation with AcCl in CH2Cl2, and (3) condensation of the amide with 3,5-diisopropyl-4-methoxybenzaldehyde. II was tested for HER-2 kinase activity (IC50 = 6.4 μM), cellular proliferation activity as measured by the incorporation of bromodeoxyuridine (BrdU) driven by HER-2 (IC50 = 9.1 μM) or EGF (IC50 = 11 μM), and antitumor activity as measured by growth of SKOV3 ovarian carcinoma cells (IC50 = 2.6 μM) or A431 human epidermoid carcinoma cells (IC50 = 2.2 μM). The invention compds. are expected to be useful in the prevention and treatment of protein kinase related cellular disorders such as cancer, diabetes, hepatic cirrhosis, cardiovascular disease, and immunol. disease.

IT **258831-72-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of 3-methylidenyl-2-indolinones as protein kinase
modulators for the prevention and treatment of cancer, diabetes, hepatic cirrhosis, cardiovascular disease, and immunol. disease)

RN 258831-72-0 CAPLUS

CN Carbamic acid, [2,3-dihydro-3-(1H-indol-2-ylmethylene)-2-oxo-1H-indol-5-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



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258830-65-8P 258830-66-9P 258830-68-1P
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258830-78-3P 258830-79-4P 258830-83-0P
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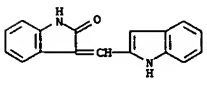
258830-94-3P 258830-95-4P 258830-96-5P
258830-97-6P 258830-98-7P 258830-99-8P
258831-00-4P 258831-01-5P 258831-02-6P
258831-04-8P 258831-05-9P 258831-08-2P
258831-09-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of 3-methylidenyl-2-indolinones as protein kinase modulators for the prevention and treatment of cancer, diabetes, hepatic cirrhosis, cardiovascular disease, and immunol. disease)

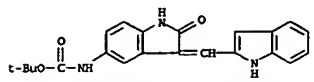
RN 22813-86-1 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(1H-indol-2-ylmethylene)- (9CI) (CA INDEX NAME)



RN 245036-10-6 CAPLUS

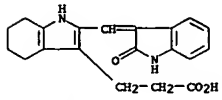
CN 1H-Indole-3-propanoic acid, 2-[[1,2-dihydro-6-(3-methoxyphenyl)-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)



IT **245036-29-7P 258831-06-0P 258831-07-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(target compound; preparation of 3-methylidenyl-2-indolinones as protein kinase modulators for the prevention and treatment of cancer, diabetes, hepatic cirrhosis, cardiovascular disease, and immunol. disease)

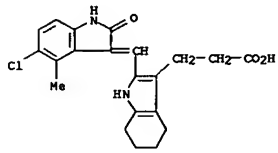
RN 245036-29-7 CAPLUS

CN 1H-Indole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)



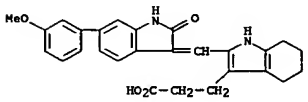
RN 258831-06-0 CAPLUS

CN 1H-Indole-3-propanoic acid, 2-[(5-chloro-1,2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)



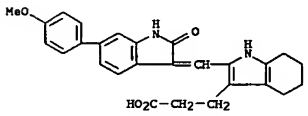
RN 258831-07-1 CAPLUS

CN 1H-Indole-3-propanoic acid, 2-[(5-bromo-1,2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)



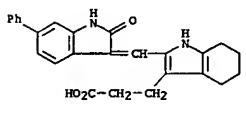
RN 245036-15-1 CAPLUS

CN 1H-Indole-3-propanoic acid, 2-[[1,2-dihydro-6-(4-methoxyphenyl)-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)



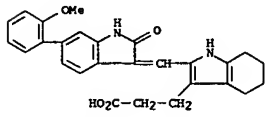
RN 245036-16-2 CAPLUS

CN 1H-Indole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-6-phenyl-3H-indol-3-ylidene)methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)



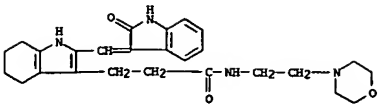
RN 245036-17-3 CAPLUS

CN 1H-Indole-3-propanoic acid, 2-[[1,2-dihydro-6-(2-methoxyphenyl)-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)

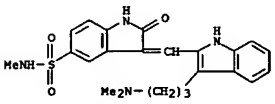


RN 245036-28-6 CAPLUS

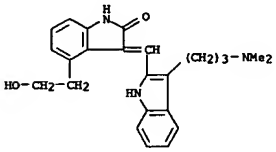
CN 1H-Indole-3-propanamide, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4,5,6,7-tetrahydro-N-[2-(4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)



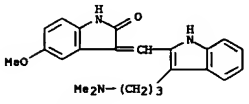
RN 258830-49-8 CAPLUS
CN 1H-Indole-5-sulfonamide, 3-[[3-[3-(dimethylamino)propyl]-1H-indol-2-yl]methylene]-2,3-dihydro-N-methyl-2-oxo- (9CI) (CA INDEX NAME)



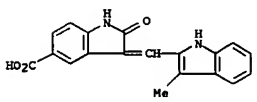
RN 258830-51-2 CAPLUS
CN 2H-Indol-2-one, 3-[[3-[3-(dimethylamino)propyl]-1H-indol-2-yl]methylene]-1,3-dihydro-4-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)



RN 258830-53-4 CAPLUS
CN 2H-Indol-2-one, 3-[[3-[3-(dimethylamino)propyl]-1H-indol-2-yl]methylene]-1,3-dihydro-5-methoxy- (9CI) (CA INDEX NAME)



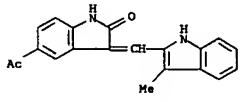
RN 258830-55-6 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-5-methyl-3-[(3-methyl-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



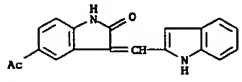
CM 2

CRN 110-89-4
CMF C5 H11 N

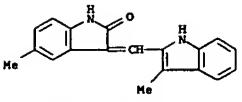
RN 258830-64-7 CAPLUS
CN 2H-Indol-2-one, 5-acetyl-1,3-dihydro-3-[(3-methyl-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



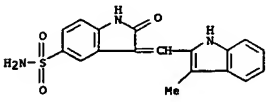
RN 258830-65-8 CAPLUS
CN 2H-Indol-2-one, 5-acetyl-1,3-dihydro-3-(1H-indol-2-ylmethylene)- (9CI) (CA INDEX NAME)



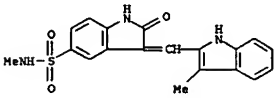
RN 258830-66-9 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-3-(1H-indol-2-ylmethylene)-2-oxo- (9CI) (CA INDEX NAME)



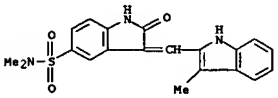
RN 258830-57-8 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-3-[(3-methyl-1H-indol-2-yl)methylene]-2-oxo- (9CI) (CA INDEX NAME)



RN 258830-59-0 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N-methyl-3-[(3-methyl-1H-indol-2-yl)methylene]-2-oxo- (9CI) (CA INDEX NAME)



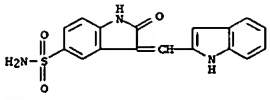
RN 258830-61-4 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N,N-dimethyl-3-[(3-methyl-1H-indol-2-yl)methylene]-2-oxo- (9CI) (CA INDEX NAME)



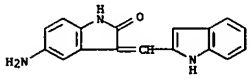
RN 258830-63-6 CAPLUS
CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-3-[(3-methyl-1H-indol-2-yl)methylene]-2-oxo-, compd. with piperidine (1:1) (9CI) (CA INDEX NAME)

CM 1

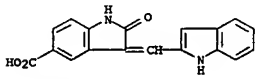
CRN 258830-62-5
CMF C19 H14 N2 O3



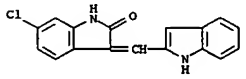
RN 258830-68-1 CAPLUS
CN 2H-Indol-2-one, 5-amino-1,3-dihydro-3-(1H-indol-2-ylmethylene)- (9CI) (CA INDEX NAME)



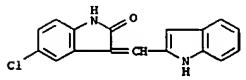
RN 258830-69-2 CAPLUS
CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-3-(1H-indol-2-ylmethylene)-2-oxo- (9CI) (CA INDEX NAME)



RN 258830-70-5 CAPLUS
CN 2H-Indol-2-one, 6-chloro-1,3-dihydro-3-(1H-indol-2-ylmethylene)- (9CI) (CA INDEX NAME)

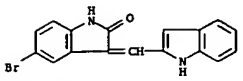


RN 258830-71-6 CAPLUS
CN 2H-Indol-2-one, 5-chloro-1,3-dihydro-3-(1H-indol-2-ylmethylene)- (9CI) (CA INDEX NAME)

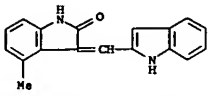


RN 258830-72-7 CAPLUS
CN 2H-Indol-2-one, 5-bromo-1,3-dihydro-3-(1H-indol-2-ylmethylene)- (9CI) (CA

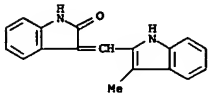
INDEX NAME)



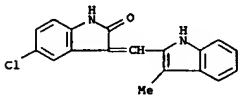
RN 258830-73-8 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-3-(1H-indol-2-ylmethylene)-4-methyl- (9CI) (CA INDEX NAME)



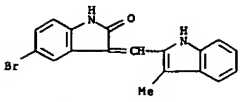
RN 258830-74-9 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-3-[(3-methyl-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



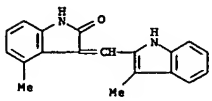
RN 258830-75-0 CAPLUS
CN 2H-Indol-2-one, 5-chloro-1,3-dihydro-3-[(3-methyl-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



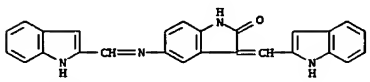
RN 258830-76-1 CAPLUS
CN 2H-Indol-2-one, 5-bromo-1,3-dihydro-3-[(3-methyl-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



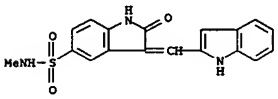
RN 258830-77-2 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-4-methyl-3-[(3-methyl-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



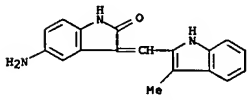
RN 258830-78-3 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-3-(1H-indol-2-ylmethylene)-5-[(1H-indol-2-ylmethylene)amino]- (9CI) (CA INDEX NAME)



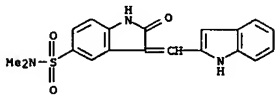
RN 258830-79-4 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-3-(1H-indol-2-ylmethylene)-N-methyl-2-oxo- (9CI) (CA INDEX NAME)



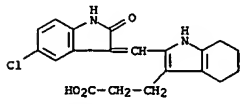
RN 258830-83-0 CAPLUS
CN 2H-Indol-2-one, 5-amino-1,3-dihydro-3-[(3-methyl-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



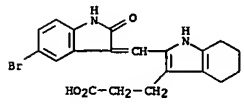
RN 258830-88-5 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-3-(1H-indol-2-ylmethylene)-N,N-dimethyl-2-oxo- (9CI) (CA INDEX NAME)



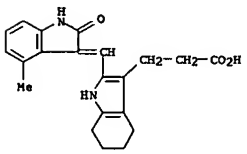
RN 258830-92-1 CAPLUS
CN 1H-Indole-3-propanoic acid, 2-[(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)



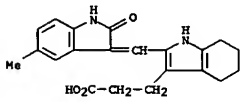
RN 258830-93-2 CAPLUS
CN 1H-Indole-3-propanoic acid, 2-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)



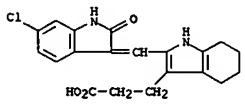
RN 258830-94-3 CAPLUS
CN 1H-Indole-3-propanoic acid, 2-[(1,2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)



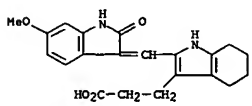
RN 258830-95-4 CAPLUS
CN 1H-Indole-3-propanoic acid, 2-[(1,2-dihydro-5-methyl-2-oxo-3H-indol-3-ylidene)methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)



RN 258830-96-5 CAPLUS
CN 1H-Indole-3-propanoic acid, 2-[(6-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)

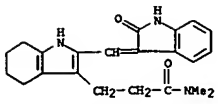


RN 258830-97-6 CAPLUS
CN 1H-Indole-3-propanoic acid, 2-[(1,2-dihydro-6-methoxy-2-oxo-3H-indol-3-ylidene)methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)

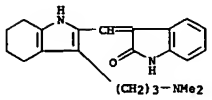


RN 258830-98-7 CAPLUS
CN 1H-Indole-3-propanamide, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4,5,6,7-tetrahydro-N,N-dimethyl- (9CI) (CA INDEX NAME)

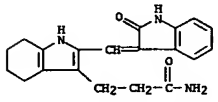
L4 ANSWER 27 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



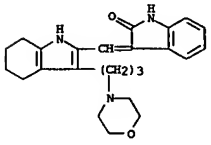
RN 258830-99-8 CAPLUS
CN 2H-Indol-2-one, 3-[[3-[3-(dimethylamino)propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)



RN 258831-00-4 CAPLUS
CN 1H-Indole-3-propanamide, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)

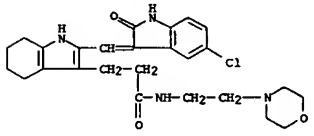


RN 258831-01-5 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-3-[[4,5,6,7-tetrahydro-3-[3-(4-morpholinyl)propyl]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

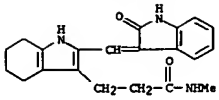


RN 258831-02-6 CAPLUS
CN 1H-Indole-3-propanamide, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4,5,6,7-tetrahydro-N-methyl- (9CI) (CA INDEX NAME)

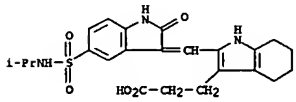
L4 ANSWER 27 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



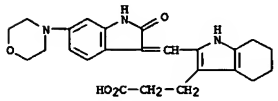
L4 ANSWER 27 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



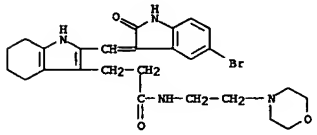
RN 258831-04-8 CAPLUS
CN 1H-Indole-3-propanoic acid, 2-[[1,2-dihydro-5-[[(1-methylethyl)amino]sulfonyl]-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)



RN 258831-05-9 CAPLUS
CN 1H-Indole-3-propanoic acid, 2-[[1,2-dihydro-6-(4-morpholinyl)-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)



RN 258831-08-2 CAPLUS
CN 1H-Indole-3-propanamide, 2-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4,5,6,7-tetrahydro-N-[2-(4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 258831-09-3 CAPLUS
CN 1H-Indole-3-propanamide, 2-[(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4,5,6,7-tetrahydro-N-[2-(4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 27 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

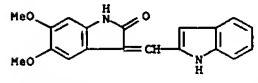
L4 ANSWER 28 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:64436 CAPLUS
DOCUMENT NUMBER: 132:342905
TITLE: Inhibition of transforming activity of the ret/ptc1 oncoprotein by a 2-indolinone derivative
AUTHOR(S): Lanzi, Cinzia; Cassinelli, Giuliana; Pensa, Tiziana; Cassinis, Marco; Gambetta, Romolo A.; Borrello, Maria G.; Menta, Ernesto; Pierotti, Marco A.; Zunino, Franco
CORPORATE SOURCE: Division of Experimental Oncology B, Istituto Nazionale Tumori, Milan, 20133, Italy
SOURCE: International Journal of Cancer (2000), 85(3), 384-390
CODEN: IJCNAW; ISSN: 0020-7136
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Ret-derived oncogenes are frequently and specifically expressed in thyroid tumors. In contrast to the ret receptor, ret oncoproteins are characterized by ligand-independent tyrosine-kinase activity and tyrosine phosphorylation. In this study, novel synthetic arylidene 2-indolinone compds. were evaluated as inhibitors of the ret/ptc1 tyrosine kinase. Four compds. inhibited ret/ptc1 activity in immunokinase assay (IC50 27-42 μM) including one (1,3-dihydro-5,6-dimethoxy-3-[(4-hydroxyphenyl) methylene]-2H-indol-2-one) (Cpd I) that selectively inhibited the anchorage-independent growth of NIH3T3 transformants expressing the ret/ptc1 gene (NIH3T3ptc1 cells). Following exposure to Cpd I, the transformed phenotype of NIH3T3ptc1 cells was reverted, within 24 h, to a normal fibroblast-like morphol. in adherent-cell culture. In these cells, the constitutive tyrosine phosphorylation of ret/ptc1, of the transducing adaptor protein shc and of a series of co-immunopptd. peptides became much reduced, as demonstrated by immunopptn./Western-blot analyses. Data presented provide addnl. evidence that ret/ptc1 is directly implicated in malignant transformation, and demonstrate the ability of Cpd I to interfere in the signal transduction pathway constitutively activated by the ret/ptc1 oncoprotein. These results confirm the interest of the arylidene 2-indolinone class of tyrosine-kinase inhibitors as tools for the study of ret signaling and the control of cell proliferation in ret- and ret/ptc1-associated diseases.

IT 269730-08-7
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of transforming activity of ret/ptc1 oncoprotein by 2-indolinone derivs.)

RN 269730-08-7 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-3-(1H-indol-2-ylmethylene)-5,6-dimethoxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 29 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:626172 CAPLUS
DOCUMENT NUMBER: 131:257441
TITLE: Heterocyclic families of compounds [tricyclic-based indolinones and pyrazolecarboxylic acid amides] for the modulation of tyrosine protein kinase
INVENTOR(S): Fong, Annie; Hannah, Alison; Harris, David G.; Hirth, Peter; Hubbard, Steven R.; Langecker, Peter; Liang, Congxin; McMahon, Gerald; Mohammadi, Moosa; Schlessinger, Joseph; Shawver, Laura K.; Sun, Li; Tang, Peng C.; Ullrich, Axel
PATENT ASSIGNEE(S): Sugen, Inc., USA; New York University; Max-Planck Institut fur Biochemie
SOURCE: PCT Int. Appl., 269 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9948868	A2	19990930	WO 1999-US6468	19990326
WO 9948868	A3	20000224		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2325935	AA	19990930	CA 1999-2325935	19990326
AU 9933635	A1	19991018	AU 1999-33635	19990326
EP 1066257	A2	20010110	EP 1999-915018	19990326
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002507598	T2	20020312	JP 2000-537851	19990326
US 6514981	B1	20030204	US 1999-283657	19990401
US 2003203901	A1	20031030	US 2002-302932	20021125

PRIORITY APPLN. INFO.: US 1998-79713P P 19980326
US 1998-80422P P 19980402
US 1998-81792P P 19980415
US 1998-82056P P 19980416
US 1998-89397P P 19980615
US 1998-89521P P 19980616
US 1998-98783P P 19980901
WO 1999-US6468 W 19990326
US 1999-283657 A3 19990401

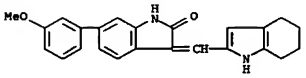
OTHER SOURCE(S): MARPAT 131:257441
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

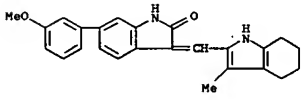
AB The invention relates to certain indolinone-based and pyrazolylamide-based compds., I and II, their method of synthesis, and combinatorial libraries consisting of the compds. [wherein AB = atoms to make up 1-2 fused and/or connected rings; R = aromatic or heteroarom. ring which may form an addnl. ring by cyclization to the methylene group; R1, R2 = H, alkyl, (hetero)aryl or -aliph. ring, amino, NO2, halo, etc.; R3 = (un)substituted Ph; Z = (un)substituted (CH2)0-3; R4, R5 = H, alkyl, (hetero)aryl or -aliph., amine, ketone, etc.]. The invention also relates to methods of modulating the function of protein kinases using these compds., and methods of treating diseases by modulating the function of protein kinases and related signal transduction pathways. Data for prepns. and/or biol. activity are given, as well as the prepns. of various oxindole intermediates. For instance, the pyrazolecarboxamide deriv. III gave up to 70% inhibition of growth of Calu-6 human lung carcinoma cells as a xenograft in mice. As another example, the indolinone deriv. IV was prepd. by condensation of 6-(4-methoxyphenyl)-2-oxindole with 3,5-dimethyl-1H-pyrrole-2-carboxaldehyde in the presence of piperidine. Extensive tests of a few selected compds. against a variety of protein kinases are described.

IT **245035-88-5P**, 6-(3-Methoxyphenyl)-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]-1,3-dihydroindol-2-one **245035-93-2P**, 6-(3-Methoxyphenyl)-3-[(3-methyl-4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]-1,3-dihydroindol-2-one **245035-96-5P**, 6-(3-Ethoxyphenyl)-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]-1,3-dihydroindol-2-one **245036-00-4P**, 6-Phenyl-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]-1,3-dihydroindol-2-one **245036-07-1P**, 6-(4-Methoxyphenyl)-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]-1,3-dihydroindol-2-one **245036-08-2P**, 6-(4-Methoxyphenyl)-3-[(3-methyl-4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]-1,3-dihydroindol-2-one **245036-10-6P**, 3-[2-[[6-(3-Methoxyphenyl)-2-oxo-1,2-dihydroindol-3-ylidene]methyl]-4,5,6,7-tetrahydro-1H-indol-3-yl]propionic acid **245036-15-1P**, 3-[2-[[6-(4-Methoxyphenyl)-2-oxo-1,2-dihydroindol-3-ylidene]methyl]-4,5,6,7-tetrahydro-1H-indol-3-yl]propionic acid **245036-16-2P**, 3-[2-[(2-Oxo-6-phenyl-1,2-dihydroindol-3-ylidene)methyl]-4,5,6,7-tetrahydro-1H-indol-3-yl]propionic acid **245036-17-3P**, 3-[2-[[6-(2-Methoxyphenyl)-2-oxo-1,2-dihydroindol-3-ylidene]methyl]-4,5,6,7-tetrahydro-1H-indol-3-yl]propionic acid **245036-21-9P**, 6-(2-Methoxyphenyl)-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]-1,3-dihydroindol-2-one **245036-22-0P**, 6-(2-Methoxyphenyl)-3-[(3-methyl-4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]-1,3-dihydroindol-2-one **245036-28-6P**, N-(2-Morpholin-4-ylethyl)-3-[2-[(2-oxo-1,2-dihydroindol-3-ylidene)methyl]-4,5,6,7-tetrahydro-1H-indol-3-yl]propionamide **245036-29-7P**, 3-[2-[(2-Oxo-1,2-dihydroindol-3-ylidene)methyl]-4,5,6,7-tetrahydro-1H-indol-3-yl]propionic acid
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of pyrazolecarboxylic acid amides and (arylmethylene)indolinones as protein tyrosine kinase modulators)

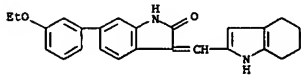
RN 245035-88-5 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-6-(3-methoxyphenyl)-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



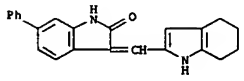
RN 245035-93-2 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-6-(3-methoxyphenyl)-3-[(4,5,6,7-tetrahydro-3-methyl-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



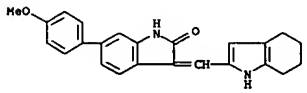
RN 245035-96-5 CAPLUS
CN 2H-Indol-2-one, 6-(3-ethoxyphenyl)-1,3-dihydro-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



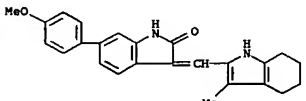
RN 245036-00-4 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-6-phenyl-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



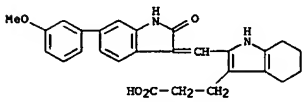
RN 245036-07-1 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-6-(4-methoxyphenyl)-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



RN 245036-08-2 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-6-(4-methoxyphenyl)-3-[(4,5,6,7-tetrahydro-3-methyl-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



RN 245036-10-6 CAPLUS
CN 1H-Indole-3-propanoic acid, 2-[[1,2-dihydro-6-(3-methoxyphenyl)-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)



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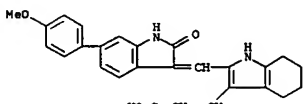
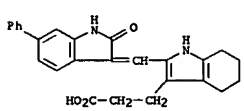
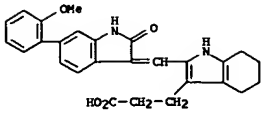


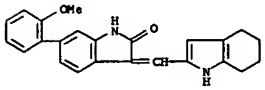
RN 245036-16-2 CAPLUS
CN 1H-Indole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-6-phenyl-3H-indol-3-ylidene)methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)



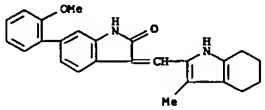
RN 245036-17-3 CAPLUS
CN 1H-Indole-3-propanoic acid, 2-[[1,2-dihydro-6-(2-methoxyphenyl)-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)



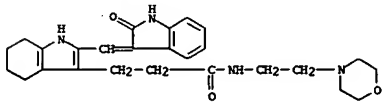
RN 245036-21-9 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-6-(2-methoxyphenyl)-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



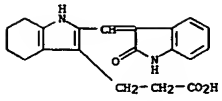
RN 245036-22-0 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-6-(2-methoxyphenyl)-3-[(4,5,6,7-tetrahydro-3-methyl-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



RN 245036-28-6 CAPLUS
CN 1H-Indole-3-propanamide, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4,5,6,7-tetrahydro-N-[2-(4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 245036-29-7 CAPLUS
CN 1H-Indole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)

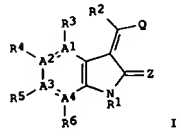


ACCESSION NUMBER: 1998:747592 CAPLUS
DOCUMENT NUMBER: 130:3771
TITLE: Preparation of 3-(hetero)arylmethylidene-2-indolinone derivatives as modulators of protein kinase activity for use in treating cancer.
INVENTOR(S): Tang, Peng Cho; Sun, Li; McMahon, Gerald; Shawver, Laura Kay; Hirth, Klaus Peter
PATENT ASSIGNEE(S): Sugen, Inc., USA
SOURCE: PCT Int. Appl., 269 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9850356	A1	19981112	WO 1998-US9017		19980507
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
CA 2289102	AA	19981112	CA 1998-2289102		19980507
AU 9876842	A1	19981127	AU 1998-76842		19980507
EP 984930	A1	20000315	EP 1998-924746		19980507
EP 984930	B1	20050406			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
JP 2002511852	T2	20020416	JP 1998-548319		19980507
AT 292623	E	20050415	AT 1998-924746		19980507
US 6051593	A	20000418	US 1998-99721		19980619
US 6313158	B1	20011106	US 1998-100854		19980619
US 6133305	A	20001017	US 1998-161046		19980925
US 2001056094	A1	20011227	US 2000-482198		20000112
US 2001007033	A1	20010705	US 2000-516948		20000301
US 2002026053	A1	20020228	US 2001-916331		20010730
US 6506763	B2	20030114			
US 2002058661	A1	20020516	US 2001-948106		20010907
US 6696463	B2	20040224			
US 2002183370	A1	20021205	US 2001-29946		20011231
US 6579897	B2	20030617			
US 2004106630	A1	20040603	US 2003-725079		20031202
US 2004106618	A1	20040603	US 2003-725267		20031202
PRIORITY APPLN. INFO.:			US 1997-45838P	P	19970507
			US 1997-46868P	P	19970508
			US 1997-49324P	P	19970611
			US 1997-50412P	P	19970620
			US 1997-50413P	P	19970620
			US 1997-50977P	P	19970620
			US 1997-59336P	P	19970919
			US 1997-59381P	P	19970919
			US 1997-59384P	P	19970919
			US 1997-59544P	P	19970919
			US 1997-59677P	P	19970919
			US 1997-59971P	P	19970925
			US 1997-60194P	P	19970926

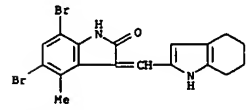
	US 1998-74621	A3	19980507
	WO 1998-US9017	W	19980507
	US 1998-100854	A3	19980619
	US 1998-99721	A1	19980619
	US 1998-161046	A3	19980925
	US 2000-482198	A3	20000112
	US 2000-516948	B1	20000301
	US 2001-819698	A3	20010329

OTHER SOURCE(S): MARPAT 130:3771
GI



I

AB Title compds. (I; A1-A4 = C, N; when any of A1-A4 = N, then the corresponding R3-R6 = null; R1 = H, alkyl, cycloalkyl, alkenyl, alkynyl, aryl, heteroaryl, heteroalicyclyl, trihalomethylcarbonyl, OH, CO2H, trihalomethylsulfonyl, etc.; R2 = H, alkyl, cycloalkyl, aryl, heteroaryl, heteroalicyclyl, halo; R3-R6 = H, alkyl, trihalomethyl, cycloalkyl, alkenyl, alkynyl, aryl, heteroaryl, heteroalicyclyl, OH, SH, alkoxy, aryloxy, amino, phosphonyl, guanidinyl, NO2, halo, (iso)cyanato, etc.; R3R4 or R4R5 or R5R6 = cycloalkyl, aryl, heteroaryl, heteroalicyclyl, OCH2O, OCH2CH2O; Q = specified (substituted) (hetero)aryl; Z = O, S], were prepared Thus, 3-(4-imidazolylmethylidenyl)-4,6-dimethyl-2-indolinone inhibited CDK2 with IC50 = <0.78 μM.
IT 215537-21-6
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of 3-(hetero)arylmethylidene-2-indolinone derivs. as modulators
of protein kinase activity for use in treating cancer)
RN 215537-21-6 CAPLUS
CN 2H-Indol-2-one, 5,7-dibromo-1,3-dihydro-4-methyl-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

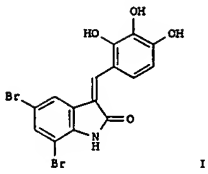
ACCESSION NUMBER: 1998:147306 CAPLUS
DOCUMENT NUMBER: 128:204803
TITLE: Indolinone combinatorial libraries and related products and methods for the treatment of disease
INVENTOR(S): Tang, Peng Cho; Sun, Li; McMahon, Gerald; Hirth, Klaus Peter; Shawver, Laura Kay; et al.
PATENT ASSIGNEE(S): Sugen, Inc., USA; Tang, Peng Cho; Sun, Li; McMahon, Gerald
SOURCE: PCT Int. Appl., 293 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9807695	A1	19980226	WO 1997-US14736	19970820
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CN 1155838	A	19970730	CN 1996-190616	19960605
CA 2264220	AA	19980226	CA 1997-2264220	19970820
EP 929520	A1	19990721	EP 1997-939480	19970820
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001503736	T2	20010321	JP 1998-510973	19970820
EP 1247803	A2	20021009	EP 2002-77564	19970820
EP 1247803	A3	20021016		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
AU 9741556	A1	19980306	AU 1997-41556	19970821

PRIORITY APPLN. INFO.:

US 1996-702232	A	19960823
US 1996-31585P	P	19961205
US 1996-31586P	P	19961205
US 1996-31588P	P	19961205
US 1996-32546P	P	19961205
US 1996-32547P	P	19961205
US 1997-45565P	P	19970505
US 1997-45566P	P	19970505
US 1997-45714P	P	19970505
US 1997-45715P	P	19970505
US 1997-46843P	P	19970505
EP 1997-939480	A3	19970820
WO 1997-US14736	W	19970820

OTHER SOURCE(S): MARPAT 128:204803
GI

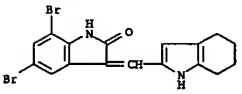


I

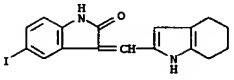
AB The invention relates to indolinone derivs. capable of modulating, regulating, and/or inhibiting protein kinase signal transduction. The compds. are useful for the treatment of diseases related to unregulated protein kinase signal transduction, including cell proliferative diseases such as cancer, atherosclerosis, arthritis, and restenosis, and metabolic diseases such as diabetes. Inhibitors specific to the FLK protein kinase can be obtained by adding chemical substituents to the 3-[(indole-3-yl)methylene]-2-indolinone system, in particular at the 1' position of the indole ring. Indolinone compds. that specifically inhibit the FLK and platelet derived growth factor protein kinases can harbor a tetrahydroindole or cyclopentano[b]pyrrole moiety. Indolinone compds. that are modified with substituents, particularly at the 5 position of the oxindole ring, can effectively activate protein kinases. This invention also features novel hydrosol. indolinone compds. that are tyrosine kinase inhibitors, and related products and methods. Approx. 1200 title compds., such as I, were prepared by combinatorial condensation of certain (un)substituted indolinones with aldehydes at the 3-position. I gave complete inhibition of MET kinase at chimeric MET receptors in vitro.

IT **203991-59-7P**, 3-[(4,5,6,7-Tetrahydroindol-2-yl)methylidenyl]-5,7-dibromo-2-indolinone **203991-69-9P**, 3-[(4,5,6,7-Tetrahydroindol-2-yl)methylidenyl]-5-iodo-2-indolinone **203991-79-1P**, 3-[(4,5,6,7-Tetrahydroindol-2-yl)methylidenyl]-5-bromo-4-methyl-2-indolinone **203991-89-3P**, 3-[(4,5,6,7-Tetrahydroindol-2-yl)methylidenyl]-5-[(methylamino)sulfonyl]-2-indolinone **203991-99-5P**, 3-[(4,5,6,7-Tetrahydroindol-2-yl)methylidenyl]-5-[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone **203992-09-0P**, 3-[(4,5,6,7-Tetrahydroindol-2-yl)methylidenyl]-5-(morpholinosulfonyl)-2-indolinone **203992-19-2P**, 3-[(4,5,6,7-Tetrahydroindol-2-yl)methylidenyl]-5-(2-chloroethyl)-2-indolinone **204003-84-9P** **204003-85-0P** **204003-88-3P** **204003-89-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and testing of indolinone combinatorial library as protein kinase inhibitors)

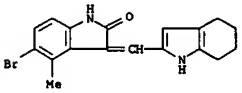
RN 203991-59-7 CAPLUS
CN 2H-Indol-2-one, 5,7-dibromo-1,3-dihydro-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



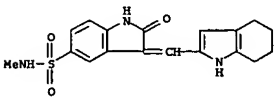
RN 203991-69-9 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-5-iodo-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



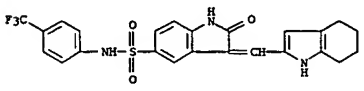
RN 203991-79-1 CAPLUS
CN 2H-Indol-2-one, 5-bromo-1,3-dihydro-4-methyl-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



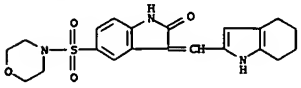
RN 203991-89-3 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N-methyl-2-oxo-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



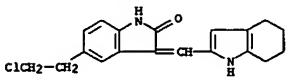
RN 203991-99-5 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-2-oxo-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



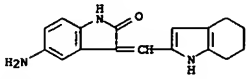
RN 203992-09-0 CAPLUS
CN Morpholine, 4-[[2,3-dihydro-2-oxo-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]-1H-indol-5-yl]sulfonyl]- (9CI) (CA INDEX NAME)



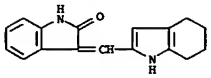
RN 203992-19-2 CAPLUS
CN 2H-Indol-2-one, 5-(2-chloroethyl)-1,3-dihydro-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



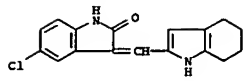
RN 204003-84-9 CAPLUS
CN 2H-Indol-2-one, 5-amino-1,3-dihydro-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



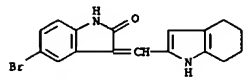
RN 204003-85-0 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



RN 204003-88-3 CAPLUS
CN 2H-Indol-2-one, 5-chloro-1,3-dihydro-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)



RN 204003-89-4 CAPLUS
CN 2H-Indol-2-one, 5-bromo-1,3-dihydro-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)

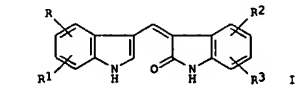


REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

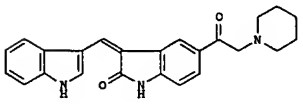
ACCESSION NUMBER: 1996:746204 CAPLUS
DOCUMENT NUMBER: 126:18783
TITLE: Substituted indolylmethylene-oxindole analogs as tyrosine kinase inhibitors
INVENTOR(S): Battistini, Carlo; Ballinari, Dario; Ermoli, Antonella; Penco, Sergio; Vioglio, Sergio
PATENT ASSIGNEE(S): Pharmacia S.P.A., Italy
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9632380	A1	19961017	WO 1996-EP1165		19960314
W: JP, US					
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
EP 764152	A1	19970326	EP 1996-907500		19960314
EP 764152	B1	20020731			
R: DE, ES, FR, GB, IT, SE					
JP 10501821	T2	19980217	JP 1996-530667		19960314
ES 2181875	T3	20030301	ES 1996-907500		19960314
US 5849710	A	19981215	US 1996-750208		19961204
PRIORITY APPLN. INFO.:			GB 1995-7298	A	19950407
			WO 1996-EP1165	W	19960314

OTHER SOURCE(S): MARPAT 126:18783
GI



I



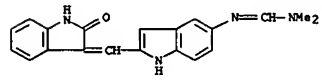
II

AB Indol-3-ylmethylene-2-oxindole derivs. I and their pharmaceutically acceptable salts are disclosed [wherein 1 or 2 of R, R1, R2, and R3 = X(CH2)mNH2, X(CH2)mNR4R5, X(CH2)mNHR6, NHC(:NH)NH2, NHC(:NH)NR4R5, NHC(:NH)NHR6, N:CHNH2, N:CHNR4R5, N:CHNHR6, X(CH2)mCOR7, CORa, COR8, YCOY'R9, NHR6, NHR10 group; remaining groups within R and R1-R3 = H, halo, amino, OH, alkyl, alkoxy, CO2H, alkoxycarbonyl, alkanoyloxy, cyano, NR4R5; X = O, S, NH; m = 1-4; 1 of R4 and R5 = H or alkyl, and other = alkyl; or NR4R5 forms saturated monoheterocycle; R6 = alkanoyl, 1- to 3-residue (un)substituted peptidyl; R7 = OH, amino, alkoxy, NR4R5; Ra = amino terminus of 1- to 3-unit peptidyl; R8 = alkoxy, phenylalkoxy, (CH2)nNH2, (CH2)nNR4R5, (CH2)nNHR6; n = 1-2; Y, Y' = NH, O; R9 = Ph, alkyl, phenylalkyl; R10 = mono-, di- or trihydroxyalkyl]. I have tyrosine kinase

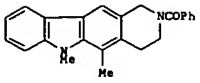
inhibiting activity, and are useful as antiproliferative, antimetastatic, anticancer, antiatheromatous, anti-Alzheimer, and immunomodulating agents. For example, 2-indolinone reacted with BrCH2COBr and AlCl3 to give the 5-(2-bromoacetyl) deriv., which underwent amination with piperidine and then condensation with indole-3-carboxaldehyde, to give title compd. II (FCE 28484). In tests for inhibition of p45 v-abl kinase and K562 leukemia cells in vitro, II had IC50 of 0.78 and 4.82 μM, resp.

IT 184020-79-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (indolylmethylene)oxindole analogs as tyrosine kinase inhibitors)

RN 184020-79-9 CAPLUS
CN Methanimidamide, N'-[2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-1H-indol-5-yl]-N,N-dimethyl- (9CI) (CA INDEX NAME)

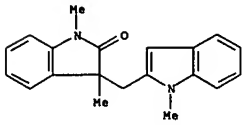


L4 ANSWER 33 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:427382 CAPLUS
DOCUMENT NUMBER: 123:33475
TITLE: Palladium-catalyzed tandem cyclization-cross-coupling reaction with triethyl(1-methylindol-2-yl)borate
AUTHOR(S): Ishikura, Minoru
CORPORATE SOURCE: Fac. Pharm. Sci., Health Sci. Univ. Hokkaido, Hokkaido, 061-02, Japan
SOURCE: Journal of the Chemical Society, Chemical Communications (1995), (4), 409-10
CODEN: JCCCAT; ISSN: 0022-4936
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 123:33475
GI



I

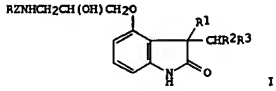
AB Triethyl(1-methylindol-2-yl)borate is successfully applied for the palladium-catalyzed tandem cyclization-cross-coupling reaction, which is used for a concise access to ellipticine derivs., e.g. I.
IT **163977-07-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(palladium-catalyzed tandem cyclization-cross-coupling reaction with triethyl(methylindolyl)borate)
RN 163977-07-9 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-1,3-dimethyl-3-[(1-methyl-1H-indol-2-yl)methyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 34 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1985:131907 CAPLUS
DOCUMENT NUMBER: 102:131907
TITLE: 2-Indolinone derivatives, pharmaceuticals containing them, and their intermediate products
INVENTOR(S): Michel, Helmut; Marzenell, Klaus; Kampe, Wolfgang; Bartsch, Wolfgang; Schaumann, Wolfgang
PATENT ASSIGNEE(S): Boehringer Mannheim G.m.b.H. , Fed. Rep. Ger.
SOURCE: Ger. Offen., 35 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3310891	A1	19840927	DE 1983-3310891	19830325
EP 121176	A1	19841010	EP 1984-103045	19840320
EP 121176	B1	19870930		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
AT 30021	E	19871015	AT 1984-103045	19840320
JP 59176253	A2	19841005	JP 1984-54612	19840323
US 4642309	A	19870210	US 1985-780704	19850926
PRIORITY APPLN. INFO.:			DE 1983-3310891 A	19830325
			EP 1984-103045 A	19840320
			US 1984-592616 A1	19840323

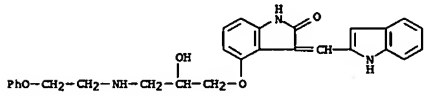
OTHER SOURCE(S): CASREACT 102:131907
GI



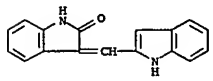
I

AB Indolinones I [R = alkyl, (un)substituted Ph; R1 = R2 = H, R1R2 = bond; R3 = (un)substituted Ph, heterocyclyl; Z = alkylene, O, S, bond] were prepared as antihypertensives and β-sympatholytics (no data). Thus, Et 2-(2-oxiranylmethyl)-6-nitrobenzeneacetate was treated Me2CHNH2 and cyclized by hydrogenation over Pd-C to give 89% 4-[2-hydroxy-3-(isopropylamino)propoxy]-2-indolinone. The latter was condensed with 2-HOC6H4CHO to give 47% I (R = Me2CH, R1R2 = Z = bond, R3 = 2-HOC6H4), which was hydrogenated over Pd-C to give 34% I.BzOH (R = Me2CH, R1 = R2 = H, R3 = 2-HOC6H4, Z = bond).
IT **94533-28-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 94533-28-5 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-4-[2-hydroxy-3-[(2-phenoxyethyl)amino]propoxy]-3-(1H-indol-2-ylmethylene)- (9CI) (CA INDEX NAME)

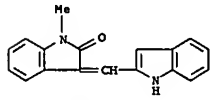
L4 ANSWER 34 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



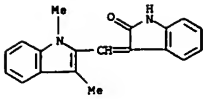
L4 ANSWER 35 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1969:403203 CAPLUS
DOCUMENT NUMBER: 71:3203
TITLE: Indole chemistry. VI. α,β'-Diindolylmethanes and α,β'-diindolylmethenes
AUTHOR(S): Von Dobeneck, Henning; Wolkenstein, Dieter; Blankenstein, Guenter
CORPORATE SOURCE: Tech. Hochsch. Muenchen, Munich, Fed. Rep. Ger.
SOURCE: Chemische Berichte (1969), 102(4), 1347-56
CODEN: CHBEAM; ISSN: 0009-2940
DOCUMENT TYPE: Journal
LANGUAGE: German
GI For diagram(s), see printed CA Issue.
AB Urorosein was prepared by polycondensation of indol-3-ylglycolic acid, followed by oxidation with the formation of the α,β'-diindolylmethene chromophore. α,β'-Diindolylmethanes (I) were prepared by the reaction of α- and β-unsubstituted indoles with glyoxylic acid; α,β'-diindolylmethenes, from α-formylindoles and β-unsubstituted indoles. Oxo-β,β'- and oxo-α,β'-diindolylmethenes were prepared from β-and α-formylindoles and oxindoles.
IT **22813-86-1P 22813-87-2P 22813-88-3P 22813-89-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 22813-86-1 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-3-(1H-indol-2-ylmethylene)- (9CI) (CA INDEX NAME)



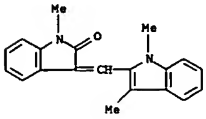
RN 22813-87-2 CAPLUS
CN 2-Indolinone, 3-(indol-2-ylmethylene)-1-methyl- (8CI) (CA INDEX NAME)



RN 22813-88-3 CAPLUS
CN 2-Indolinone, 3-[(1,3-dimethylindol-2-yl)methylene]- (8CI) (CA INDEX NAME)



RN 22813-89-4 CAPLUS
CN 2-Indolinone, 3-[(1,3-dimethylindol-2-yl)methylene]-1-methyl- (8CI) (CA INDEX NAME)



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